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 Brivaracetam (new therapeutic indication: epilepsy with partial onset seizures, adjunctive therapy, ≥ 2 to < 4 years)

of 1 September 2022

Contents

1. Legal basis

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

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

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

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

2. Key points of the resolution

The active ingredient brivaracetam (Briviact) was listed for the first time on 15 February 2016 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices.

On 24 February 2022, Briviact 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, p. 7).

On 28 February 2022, i.e. at the latest within four weeks after informing the pharmaceutical company about the approval of a new therapeutic indication, the pharmaceutical company has submitted a dossier in due time in accordance with Section 4, paragraph 3, number 2 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 brivaracetam with the new therapeutic indication (Briviact is indicated as adjunctive therapy in the treatment of partial onset seizures with or without secondary generalisation in adults, adolescents and children from 2 years of age with epilepsy).

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 1 June 2022 on the website of the G-BA (http://www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

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

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

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

2.1.1 Approved therapeutic indication of Brivaracetam (Briviact) in accordance with the product information

Briviact is indicated as adjunctive therapy in the treatment of partial onset seizures with or without secondary generalisation in adults, adolescents and children from 2 years of age with epilepsy.

Therapeutic indication of the resolution (resolution of 01.09.2022):

Adjunctive therapy in the treatment of partial onset seizures with or without secondary generalisation in children from 2 to < 4 years with epilepsy.

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Children aged 2 to < 4 years with partial onset epileptic seizures with or without secondary generalisation(s) on adjunctive therapy

Appropriate comparator therapy for brivaracetam:

- a patient-individual anti-epileptic adjunctive therapy, if medically indicated and if no pharmacoresistance (in the sense of an insufficient response), intolerance or

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

contraindication is known, taking into account the basic and previous therapy/ therapies and the reason for the change of therapy as well as any associated side effects

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

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

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

1. To be considered as a comparator therapy, the medicinal product must, principally, have a marketing authorisation for the therapeutic indication.
2. If a non-medicinal treatment is considered as a comparator therapy, this must be available within the framework of the SHI system.
3. As comparator therapy, medicinal products or non-medicinal treatments for which the patient-relevant benefit has already been determined by the G-BA shall be preferred.
4. According to the generally recognised state of medical knowledge, the comparator therapy should be part of the appropriate therapy in the therapeutic indication.

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

on 1. In the present therapeutic indication, the following active ingredients are approved for therapy in children aged 2 to < 4 years: Carbamazepine, clobazam, lacosamide, lamotrigine, levetiracetam, phenytoin, primidone, topiramate and valproic acid.

on 2. A non-medicinal treatment cannot be considered an appropriate comparator therapy in this therapeutic indication.

on 3. There are no resolutions on the adjunctive therapy of partial onset seizures in children aged 2 to < 4 years with epilepsy.

Irrespective of the age of the patients, the following resolutions of the G-BA have been made in the therapeutic indication of adjunctive therapy of partial onset seizures with or without secondary generalisation:

- Retigabine: Resolution on the benefit assessment of medicinal products with new active ingredients pursuant to Section 35a SGB V of 3 July 2014 (renewed benefit assessment based on new scientific findings). On 19 July 2018, the European Commission revoked the marketing authorisation for the active ingredient retigabine (Trobalt).
- Perampanel: Resolutions on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V of 6 November 2014 (renewed benefit assessment based on new scientific findings) and 3 June 2021 (new therapeutic indication children and adolescents ≥ 4 to < 12 years).

- Brivaracetam: Resolutions on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V of 4 August 2016 and 17 January 2019 (new therapeutic indication children and adolescents ≥ 4 to < 16 years).
- Vigabatrin: Resolution on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V of 19 November 2019 (children ≥ 1 month to < 7 years).
- Cenobamate: Resolution on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V of 19 November 2021.

on 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as reviews of clinical studies in the present therapeutic indication.

The assessment of the available evidence showed that patient-individual antiepileptic adjunctive therapy is appropriate, taking into account the baseline and previous therapy/ therapies and the reason for the change in therapy and any associated side effects, as long as this is medically indicated and if no pharmacoresistance (in the sense of an inadequate response), intolerance or contraindication is known.

For the adjunctive therapy of partial onset seizures with or without secondary generalisation in children aged 2 to < 4 years, the above-mentioned active ingredients are available according to the respective approved therapeutic indication.

Overall, the body of evidence for the treatment of children aged 2 to < 4 years with epilepsy and partial onset seizures is very limited. According to the clinical experts, the active ingredients eslicarbazepine, lacosamide, lamotrigine, levetiracetam and oxcarbazepine are primarily used in Germany in children with partial onset seizures because of their better tolerability compared to older medicinal products with more side effects such as carbamazepine, phenytoin, phenobarbital and valproic acid. In addition, recommendations on topiramate and gabapentin are available from an American guideline based on studies that include the age group of the present therapeutic indication.

The active ingredients eslicarbazepine, gabapentin and oxcarbazepine are only approved in the present indication for the treatment of children from 6 years of age. Therefore, there is a discrepancy between medicinal products approved in the indication and those used in health care/ recommended in guidelines.

In a clinical study, the following active ingredients are considered suitable comparators: Eslicarbazepine, gabapentin, lacosamide, lamotrigine, levetiracetam, oxcarbazepine and topiramate. However, the possibility of the off-label use of the active ingredients mentioned in a clinical study does not allow any conclusions to be drawn about their appropriateness in the off-label use in the standard care of insured persons in the SHI system. Such an assessment would be reserved for the decision according to Section 35c SGB V. This does not affect an off-label prescription in specific cases according to the criteria of the established case law of the Federal Social Court on off-label use not regulated in the Pharmaceuticals Directive.

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

2.1.3 Extent and probability of the additional benefit

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

An additional benefit is not proven.

Justification:

No relevant RCT comparing brivaracetam with the appropriate comparator therapy was identified for the assessment of additional benefit.

Therefore, the pharmaceutical company submits the non-comparator 1-arm N01266 study on brivaracetam. This study is a long-term study of the clinical development phase 3 in which children and adolescents who have previously participated in other studies with brivaracetam were enrolled. For children and adolescents aged ≥ 4 to < 17 years, direct enrolment in the study was also possible if they were already treated with at least 1 anticonvulsant. The N01263 and EP0065 studies are relevant precursor studies.

The N01263 study is a 1-arm phase 2a study for investigating the pharmacokinetics, safety and efficacy of brivaracetam in children and adolescents with epilepsy. Patients aged ≥ 1 month to < 16 years who were treated with at least 1 to a maximum of 3 other anticonvulsants were enrolled in the study. The enrolled patients received brivaracetam as an oral solution in addition to their existing anti-epileptic therapy.

The EP0065 study is a 1-arm phase 2 study for investigating the pharmacokinetics and safety of brivaracetam by administering a 15-minute infusion and bolus infusion thereof in children and adolescents with epilepsy. Patients aged ≥ 1 month to < 16 years treated with at least 1 anticonvulsant were enrolled in the study. All patients enrolled were administered brivaracetam intravenously for a maximum of 6 days.

Following treatment in the respective study, patients were able to transfer to the N01266 study and continue their treatment.

Patients from other studies were to continue the individual brivaracetam dose of the previous study, directly enrolled patients were administered brivaracetam in a 3-week titration phase in weekly increasing doses adjusted to body weight for a maximum of 3 weeks before they also switched to the maintenance phase. Overall, patients should be treated with brivaracetam for at least 3 years.

The pharmaceutical company submits data of the N01266 study for the benefit assessment at the data cut-off from 14 July 2020. At this time, 256 patients were enrolled in the study. However, according to the information provided by the pharmaceutical company, only 4 patients (transferred from the N01263 and EP0065 studies) correspond to the therapeutic indication relevant for the present benefit assessment with regard to age and seizure type.

Since the 1-arm N01266 study does not allow a direct comparison of brivaracetam versus the appropriate comparator therapy, the data are not suitable for assessing the additional benefit of brivaracetam. In addition, only 4 patients in the N01266 study correspond to the therapeutic indication to be assessed with regard to age and seizure type.

The pharmaceutical company therefore does not present suitable data compared to the appropriate comparator therapy for the assessment of the additional benefit of brivaracetam for the treatment of children aged 2 to < 4 years with partial onset epileptic seizures with or without secondary generalisation in the adjunctive therapy setting. An additional benefit is therefore not proven.

2.1.4 Summary of the assessment

The present assessment is the benefit assessment of a new therapeutic indication for the active ingredient brivaracetam. The therapeutic indication assessed here is as follows: "Adjunctive therapy in the treatment of partial onset seizures with or without secondary generalisation in children from 2 to < 4 years with epilepsy."

The G-BA determined the appropriate comparator therapy to be a patient-individual anti-epileptic adjunctive therapy, if medically indicated and if no pharmacoresistance (in the sense of an insufficient response), intolerance or contraindication is known, taking into account the basic and previous therapy/ therapies and the reason for the change of therapy as well as any associated side effects. In a clinical study, the active ingredients eslicarbazepine, gabapentin, lacosamide, lamotrigine, levetiracetam, oxcarbazepine and topiramate are considered suitable comparators.

For the patient group of children from 2 to < 4 years, the pharmaceutical company presents the 1-arm N01266 study. This does not allow a direct comparison of brivaracetam versus the appropriate comparator therapy. In addition, only 4 patients of the N01266 study correspond to the therapeutic indication to be assessed with regard to age and seizure type.

The pharmaceutical company therefore does not present suitable data compared to the appropriate comparator therapy for the assessment of the additional benefit of brivaracetam for the treatment of children aged 2 to < 4 years with partial onset epileptic seizures with or without secondary generalisation in the adjunctive therapy setting. An additional benefit is therefore not proven.

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 pharmaceutical company indicates a range of 300 to 900 children when deriving the patient numbers. Overall, the derivation of patient numbers is mathematically comprehensible, but subject to uncertainty. Taking into account existing uncertainties, the upper limit determined by the pharmaceutical company, in particular, is classified as underestimated. This is mainly the result of the pharmaceutical company's estimate of the percentage value for the presence of focal epilepsy. Taking into account an upper limit of 69% for the presence of focal epilepsy based on the study by Aaberg et al. [2], this results in a number of about 300 to 1,800 patients for the SHI target population.

[2] Aaberg KM, Suren P, Soraas CL et al. Seizures, syndromes, and etiologies in childhood epilepsy: The International League Against Epilepsy 1981, 1989, and 2017 classifications used in a population-based cohort. Epilepsia 2017; 58(11): 1880-1891. https://dx.doi.org/10.1111/epi.13913.

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 Briviact (active ingredient: brivaracetam) at the following publicly accessible link (last access: 27 June 2022):

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

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 August 2022).

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.

For the cost representation only the dosages of the general case are considered. Patient-individual dose adjustments (e.g., because of side effects or comorbidities) 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.

For dosages depending on body weight (BW), the average body measurements from the official representative statistics "Microcensus 2017 – body measurements of the population" were used as a basis. The average body weight of 2-year-olds (14.1 kg) and 3-year-olds (16.2 kg) was used to calculate the range of annual treatment costs.

In this particular patient population, it is up to the physician to decide which is the most appropriate dosage form for the respective child from 2 years < 4 years of age, depending on body weight and dose. For this reason, where available, the dosages of both a solid (tablet or hard capsule) and a liquid formulation (solution, suspension or syrup) are shown for each active ingredient.

If the recommended maintenance dose is given as an age-dependent range in the respective product information, the lower and upper limits of the range are calculated here in each case. If more than one treatment mode was indicated in the product information, "twice daily" was calculated for better comprehensibility.

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

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				
Brivaracetam OS and FCT	continuously, 2 x daily	365	1	365
Appropriate comparator therapy				
a patient-individual anti-epileptic adjunctive therapy [a]				
Lacosamide SYR and FCT	continuously, 2 x daily	365	1	365
Lamotrigine TOS and TAB	continuously, 1 - 2 x daily	365	1	365
Levetiracetam OS	continuously, 2 x daily	365	1	365
Topiramate FCT and HC	continuously, 2 x daily	365	1	365

[a] Costs are only presented for the active ingredients lacosamide, lamotrigine, levetiracetam and topiramate. In addition to these active ingredients, the medicinal products eslicarbazepine, gabapentin and oxcarbazepine are also suitable comparators for the present benefit assessment in the context of patient-individual therapy. However, these medicinal products are not approved in the present therapeutic indication, and therefore, no costs are presented for these medicinal products.

Abbreviations: FCT = film-coated tablets, HC = hard capsules, OS = oral solution, SYR = syrup, TAB = tablets, TOS = tablets for oral suspension

Consumption:

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Annual average consumption by potency
Medicinal product to be assessed					
Brivaracetam OS	0.5 mg/kg = 7.05 mg - 2.5 mg/kg = 40.5 mg	14.1 mg - 81 mg	2 x 7 mg [3] - 2 x 41 mg	365	730 x 7 mg - 730 x 41 mg
Brivaracetam FCT	0.5 mg/kg = 7.05 mg - 2.5 mg/kg = 40.5 mg	14.1 mg - 81 mg	2 x 10 mg - 8 x 10 mg	365	730 x 10 mg - 2920 x 10 mg
Appropriate comparator therapy					
a patient-individual anti-epileptic adjunctive therapy [a]					
Lacosamide SYR	2 mg/kg = 28.2 mg - 6 mg/kg = 97.2 mg	56.4 mg - 194.4 mg	2 x 30 mg [4] - 2 x 97.5 mg	365	730 x 30 mg - 730 x 97.5 mg
Lacosamide FCT	2 mg/kg = 28.2 mg - 6 mg/kg = 97.2 mg	56.4 mg - 194.4 mg	- [5] 2 x 100 mg	365	- 730 x 100 mg
Lamotrigine TOS	0.5 mg/kg = 7.05 mg - 7.5 mg/kg = 121.5 mg	14.1 mg - 243 mg	2 x 5 mg + 2 x 2 mg [6,7] - 2 x 100 mg + 8 x 5 mg	365	730 x 5 mg + 730 x 2 mg - 730 x 100 mg + 2920 x 5 mg

[3] The oral solution has a concentration of 10 mg/ml. According to the product information, a scaling of 0.1 ml increments is possible.

[4] The syrup has a concentration of 10 mg/ml. According to the product information, a scaling of 0.25 ml increments is possible.

[5] Lower limit not administrable with FCT.

[6] The dose range depends on whether valproate and/or inducers of glucuronidation of lamotrigine are also being taken.

[7] If the calculated dose of lamotrigine cannot be administered in whole tablets for oral suspension (TOS), the next lower dose that can be given in whole TOS should be administered.

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Annual average consumption by potency
Lamotrigine TAB	1 mg/kg = 14.1 mg - 7.5 mg/kg = 121.5 mg	14.1 mg - 243 mg	0.5 x 25 mg[8] - 2 x 100 mg + 1 x 25 mg	365	182.5 x 25 mg - 730 x 100 mg + 365 x 25 mg
Levetiracetam OS	10 mg/kg = 141 mg - 30 mg/kg = 486 mg	282 mg - 972 mg	2 x 140 mg[9] - 2 x 490 mg	365	730 x 140 mg - 730 x 490 mg
Topiramate HC	2.5 mg/kg = 35.25 mg - 4.5 mg/kg = 72.9 mg	70.5 mg - 145.8 mg	2 x 25 mg - 2 x 50 mg + 2 x 25 mg	365	730 x 25 mg - 730 x 50 mg + 730 x 25 mg
Topiramate FCT	2.5 mg/kg = 35.25 mg - 4.5 mg/kg = 72.9 mg	70.5 mg - 145.8 mg	3 x 25 mg[10] - 2 x 50 mg + 2 x 25 mg	365	1095 x 25 mg - 730 x 50 mg + 730 x 25 mg
[a] Costs are only presented for the active ingredients lacosamide, lamotrigine, levetiracetam and topiramate. In addition to these active ingredients, the medicinal products eslicarbazepine, gabapentin and oxcarbazepine are also suitable comparators for the present benefit assessment in the context of patient-individual therapy. However, these medicinal products are not approved in the present therapeutic indication, and therefore, no costs are presented for these medicinal products.					
Abbreviations: FCT = film-coated tablets, HC = hard capsules, OS = oral solution, SYR = syrup, TAB = tablets, TOS = tablets for oral suspension					

Costs:

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

[8] 25 mg tablets divisible into 2 x 12.5 mg lamotrigine at the same dose. Here, only 1 x-daily administration possible, as the smallest possible dosage would be too high with 2 x-daily administration.

[9] The oral solution has a concentration of 100 mg/ml. According to the product information, a scaling of 0.1 ml increments is possible.

[10] 25 mg film-coated tablets divisible into 4 x 6.25 mg topiramate at the same dose.

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					
Brivaracetam OS 10 mg/ml	300 ml OS	€ 114.45	€ 1.77	€ 5.71	€ 106.97
Brivaracetam FCT 10 mg	14 FCT	€ 35.35	€ 1.77	€ 1.33	€ 32.25
Appropriate comparator therapy					
a patient-individual anti-epileptic adjunctive therapy [a]					
Lacosamide SYR 10 mg/ml	200 ml SYR	€ 72.77	€ 1.77	€ 3.40	€ 67.60
Lacosamide FCT 100 mg	168 FCT	€ 424.38	€ 1.77	€ 22.87	€ 399.74
Lamotrigine TOS 2 mg [11]	30 TOS	€ 11.31	€ 1.77	€ 0.00	€ 9.54
Lamotrigine TOS 5 mg [11]	60 TOS	€ 11.53	€ 1.77	€ 0.02	€ 9.74
Lamotrigine TOS 100 mg [11]	196 TOS	€ 47.85	€ 1.77	€ 2.89	€ 43.19
Lamotrigine TAB 25 mg [11]	200 TAB	€ 19.47	€ 1.77	€ 0.65	€ 17.05
Lamotrigine TAB 100 mg [11]	200 TAB	€ 48.96	€ 1.77	€ 2.98	€ 44.21
Levetiracetam OS 100 mg/ml [11]	150 ml OS	€ 49.27	€ 1.77	€ 3.00	€ 44.50
Topiramate HC 25 mg [11]	100 HC	€ 30.02	€ 1.77	€ 1.48	€ 26.77
Topiramate HC 50 mg [11]	100 HC	€ 46.55	€ 1.77	€ 2.79	€ 41.99
Topiramate FCT 25 mg [11]	200 FCT	€ 49.72	€ 1.77	€ 3.04	€ 44.91
Topiramate FCT 50 mg [11]	200 FCT	€ 83.63	€ 1.77	€ 5.72	€ 76.14
[a] Costs are only presented for the active ingredients lacosamide, lamotrigine, levetiracetam and topiramate. In addition to these active ingredients, the medicinal products eslicarbazepine, gabapentin and oxcarbazepine are also suitable comparators for the present benefit assessment in the context of patient-individual therapy. However, these medicinal products are not approved in the present therapeutic indication, and therefore, no costs are presented for these medicinal products.					
Abbreviations: FCT = film-coated tablets, HC = hard capsules, OS = oral solution, SYR = syrup, TAB = tablets, TOS = tablets for oral suspension					

LAUER-TAXE® last revised: 15 August 2022

[11] 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, the costs incurred for this must be taken into account as costs for additionally required SHI services.

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

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

3. Bureaucratic costs calculation

The proposed resolution does not create any new or amended information obligations for care providers within the meaning of Annex II to Chapter 1 VerfO and, accordingly, no bureaucratic costs.

4. Process sequence

At its session on 8 June 2021, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 28 February 2022, the pharmaceutical company submitted a dossier for the benefit assessment of brivaracetam to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 2 VerfO.

By letter dated 28 February 2022 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefits of medicinal products with new active ingredients in accordance with Section 35a SGB V, the G-BA commissioned the IQWiG to assess the dossier concerning the active ingredient brivaracetam.

The dossier assessment by the IQWiG was submitted to the G-BA on 18 May 2022, and the written statement procedure was initiated with publication on the website of the G-BA on 1 June 2022. The deadline for submitting written statements was 22 June 2022.

The oral hearing was held on 11 July 2022.

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 23 August 2022, and the proposed resolution was approved.

At its session on 1 September 2022, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal products	8 June 2021	Determination of the appropriate comparator therapy
Working group Section 35a	6 July 2022	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal products	11 July 2022	Conduct of the oral hearing
Working group Section 35a	20 July 2022 17 August 2022	Consultation on the dossier assessment by the IQWiG, assessment of the written statement procedure
Subcommittee Medicinal products	23 August 2022	Concluding discussion of the draft resolution
Plenum	1 September 2022	Adoption of the resolution on the amendment of Annex XII AM-RL

Berlin, 1 September 2022

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

Prof. Hecken