IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

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Brivaracetam – Benefit assessment according to §35a Social Code Book V[1]

Extract

[1] Translation of Sections 2.1 to 2.6 of the dossier assessment *Brivaracetam – Nutzenbewertung gemäß § 35a SGB V* (Version 1.0; Status: 12 May 2016). Please note: This translation is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

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IQWiG thanks the medical and scientific advisor for his contribution to the dossier assessment. However, the advisor was not involved in the actual preparation of the dossier assessment. The responsibility for the contents of the dossier assessment lies solely with IQWiG.

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[2] Due to legal data protection regulations, employees have the right not to be named.

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[3] Table numbers start with "2" as numbering follows that of the full dossier assessment.

List of abbreviations

Abbreviation	Meaning
ACT	appropriate comparator therapy
AE	adverse event
AED	antiepileptic drug
EMA	European Medicines Agency
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
PT	Preferred Term
RCT	randomized controlled trial
SAE	serious adverse event
SGB	Sozialgesetzbuch (Social Code Book)
SOC	System Organ Class
SPC	Summary of Product Characteristics

2 Benefit assessment

2.1 Executive summary of the benefit assessment

Background

In accordance with §35a Social Code Book (SGB) V, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to assess the benefit of the drug brivaracetam. The assessment was based on a dossier compiled by the pharmaceutical company (hereinafter referred to as "the company"). The dossier was sent to IQWiG on 11 February 2016.

Research question

The aim of this report was to assess the added benefit of brivaracetam compared with the appropriate comparator therapy (ACT) in patients with epilepsy.

The present benefit assessment was conducted in comparison with the ACT specified by the G-BA for the research question presented in Table 2.

Table 2: Research question of the benefit assessment of brivaracetam

Research question	Therapeutic indication	Appropriate comparator therapy[a]
A	Adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalization in adult and adolescent (16–18 years) patients with epilepsy	Individual antiepileptic adjunctive treatment, if medically indicated and if no pharmacoresistance/intolerance and contraindications are known yet, with one of the following drugs: eslicarbazepine or gabapentin or lacosamide or lamotrigine or levetiracetam or oxcarbazepine or pregabalin or topiramate or valproic acid or zonisamide
a: Presentation of the appropriate comparator therapy specified by the G-BA. G-BA: Federal Joint Committee		

The company claimed to have followed the G-BA regarding the ACT, but limited its assessment to a comparison with 2 of the drugs specified by the G-BA (lacosamide and eslicarbazepine). This approach was not followed because all drugs specified by the G-BA are an option for a comprehensive individual antiepileptic adjunctive treatment. Irrespective of this, it was investigated whether, in the studies presented by the company, lacosamide or eslicarbazepine constituted the individually optimized treatment for the patients included in these studies.

The assessment was conducted based on patient-relevant outcomes and on the data provided by the company in the dossier. Studies with a minimum duration of the maintenance phase of 12 weeks were used for the derivation of the added benefit.

Results

Since studies of direct comparisons were lacking, the company used 3 indirect comparisons based on randomized controlled trials (RCTs):

- brivaracetam versus lacosamide
- brivaracetam versus eslicarbazepine
- brivaracetam versus lacosamide/eslicarbazepine (combined analysis of the studies on lacosamide and eslicarbazepine)

The company identified 6 brivaracetam studies (N01114, N01193, N01252, N01253, N01254 and N01358), 4 lacosamide studies (EP0008, SP667, SP754 and SP755) and 5 eslicarbazepine studies (BIA-2093-201, BIA-2093-301, BIA-2093-302, BIA-2093-303 and BIA-2093-304).

The respective drug was compared with placebo in all 15 studies, in each case as adjunctive treatment to ongoing basic therapy. Hence basic therapy + placebo was used as common comparator for all 3 indirect comparisons.

For the implementation of the ACT it would have been necessary to prove that the adjunctive treatment with lacosamide or eslicarbazepine in each case was the individually optimized treatment for the patients included in the studies. The company did not provide this proof. Irrespective of this, all indirect comparisons presented by the company (brivaracetam versus lacosamide and brivaracetam versus eslicarbazepine) were not usable for other reasons.

Suitability of the studies with brivaracetam

Of the 6 studies included by the company in its indirect comparisons, only study N01254 was potentially relevant for an indirect comparison. The designs of the other studies contained one or several aspects opposed to an inclusion for the benefit assessment. The aspects can be categorized as follows:

- no titration (the dose of brivaracetam was not individually titrated as recommended in the Summary of Product Characteristics [SPC]): 4 of the 5 remaining studies
- study duration too short: 2 of the 5 remaining studies

Indirect comparison of brivaracetam versus lacosamide

The indirect comparison of brivaracetam versus lacosamide was unsuitable to derive conclusions on the added benefit of brivaracetam versus lacosamide. One of the reasons for this was that the company included brivaracetam studies in this comparison that were unsuitable for the benefit assessment. Another reason was that most of the studies included by the company were not sufficiently similar for an indirect comparison. Furthermore, the indirect comparison was incomplete with regard to content because the company did not present analyses for all relevant outcomes, although the corresponding data were available.

Indirect comparison of brivaracetam versus eslicarbazepine

The indirect comparison of brivaracetam versus eslicarbazepine was unsuitable to derive conclusions on the added benefit of brivaracetam versus eslicarbazepine. One of the reasons for this was that the company included brivaracetam studies in this comparison that were unsuitable for the benefit assessment. Another reason was that, also in this case, most of the studies included by the company were not sufficiently similar for an indirect comparison. Furthermore, the indirect comparison with eslicarbazepine was also incomplete with regard to content because the company did not present analyses for all relevant outcomes for which data were available.

Indirect comparison of brivaracetam versus lacosamide/eslicarbazepine

Since both indirect comparisons of brivaracetam versus lacosamide or versus eslicarbazepine were unsuitable, the indirect comparison of brivaracetam versus lacosamide/eslicarbazepine (combined analysis) was also unsuitable to derive conclusions on the added benefit of brivaracetam in comparison with both drugs lacosamide and eslicarbazepine.

Extent and probability of added benefit, patient groups with therapeutically important added benefit[4]

On the basis of the results presented, the extent and probability of the added benefit of the drug brivaracetam compared with the ACT is assessed as follows:

An added benefit of brivaracetam is not proven because the company presented no suitable data.

Table 3 presents a summary of the extent and probability of the added benefit of brivaracetam.

[4] On the basis of the scientific data analysed, IQWiG draws conclusions on the (added) benefit or harm of an intervention for each patient-relevant outcome. Depending on the number of studies analysed, the certainty of their results, and the direction and statistical significance of treatment effects, conclusions on the probability of (added) benefit or harm are graded into 4 categories: (1) “proof”, (2) “indication”, (3) “hint”, or (4) none of the first 3 categories applies (i.e., no data available or conclusions 1 to 3 cannot be drawn from the available data). The extent of added benefit or harm is graded into 3 categories: (1) major, (2) considerable, (3) minor (in addition, 3 further categories may apply: non-quantifiable extent of added benefit, no added benefit, or less benefit). For further details see [1,2].

Table 3: Brivaracetam – extent and probability of added benefit

Therapeutic indication	**Appropriate comparator therapy**[a]	**Extent and probability of added benefit**
Adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalization in adult and adolescent (16–18 years) patients with epilepsy	Individual antiepileptic adjunctive treatment, if medically indicated and if no pharmacoresistance/intolerance and contraindications are known yet, with one of the following drugs: eslicarbazepine or gabapentin or lacosamide or lamotrigine or levetiracetam or oxcarbazepine or pregabalin or topiramate or valproic acid or zonisamide	Added benefit not proven
a: Presentation of the appropriate comparator therapy specified by the G-BA. G-BA: Federal Joint Committee		

The G-BA decides on the added benefit.

2.2 Research question

The aim of this report was to assess the added benefit of brivaracetam compared with the ACT in patients with epilepsy.

The present benefit assessment was conducted in comparison with the ACT specified by the G-BA for the research question presented in Table 4.

Table 4: Research question of the benefit assessment of brivaracetam

Research question	**Therapeutic indication**	**Appropriate comparator therapy**[a]
A	Adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalization in adult and adolescent (16–18 years) patients with epilepsy	Individual antiepileptic adjunctive treatment, if medically indicated and if no pharmacoresistance/intolerance and contraindications are known yet, with one of the following drugs: eslicarbazepine or gabapentin or lacosamide or lamotrigine or levetiracetam or oxcarbazepine or pregabalin or topiramate or valproic acid or zonisamide
a: Presentation of the appropriate comparator therapy specified by the G-BA. G-BA: Federal Joint Committee		

The company claimed to have followed the G-BA regarding the ACT, but limited its assessment to a comparison with 2 of the drugs specified by the G-BA (lacosamide and eslicarbazepine). This approach was not followed because all drugs specified by the G-BA are an option for a comprehensive individual antiepileptic adjunctive treatment. Irrespective of this, it was investigated whether, in the studies presented by the company, lacosamide or eslicarbazepine constituted the individually optimized treatment for the patients included in these studies.

The assessment was conducted based on patient-relevant outcomes and on the data provided by the company in the dossier. Studies with a minimum duration of the maintenance phase of 12 weeks were used for the derivation of the added benefit. This deviates from the company's approach, which used studies with a minimum duration of the maintenance phase of 6 weeks.

2.3 Information retrieval and study pool

The study pool of the assessment was compiled on the basis of the following information:

Sources of the company in the dossier:

- study list on brivaracetam (status: 28 December 2015)
- bibliographical literature search on brivaracetam (last search on 16 December 2015)
- search in trial registries for studies on brivaracetam (last search on 28 December 2015)
- study list on lacosamide (status: 18 December 2015)
- bibliographical literature search on lacosamide and eslicarbazepine (last search on 16 December 2015)
- search in trial registries for studies on lacosamide and eslicarbazepine (last search on 21 December 2015)

To check the completeness of the study pool:

- search in trial registries for studies on brivaracetam (last search on 23 February 2016)
- search in trial registries for studies on lacosamide (last search on 23 February 2016)

No additional relevant study was identified from the check.

Direct comparison

There were no studies of direct comparisons of brivaracetam in comparison with the ACT. This concurs with the company's assessment.

Indirect comparison

Since studies of direct comparisons were lacking, the company used 3 indirect comparisons based on RCTs:

- brivaracetam versus lacosamide
- brivaracetam versus eslicarbazepine
- brivaracetam versus lacosamide/eslicarbazepine (combined analysis of the studies on lacosamide and eslicarbazepine)

From the steps of information retrieval mentioned, the company identified 6 brivaracetam studies (N01114 [3], N01193 [4], N01252 [5], N01253 [6], N01254 [7] and N01358 [8]),

4 lacosamide studies (EP0008 [9], SP667 [10], SP754 [11] and SP755 [12]) and 5 eslicarbazepine studies (BIA-2093-201 [13], BIA-2093-301 [14], BIA-2093-302 [15], BIA-2093-303 [16] and BIA-2093-304 [17]) for this.

The respective drug was compared with placebo in all 15 studies, in each case as adjunctive treatment to ongoing basic therapy. Hence basic therapy + placebo was used as common comparator for all 3 indirect comparisons.

For the implementation of the ACT it would have been necessary to prove that the adjunctive treatment with lacosamide or eslicarbazepine in each case was the individually optimized treatment for the patients included in the studies. The company did not provide this proof. Irrespective of this, all indirect comparisons presented by the company (brivaracetam versus lacosamide and brivaracetam versus eslicarbazepine) were not usable for other reasons. The reasons are explained below.

Suitability of the studies with brivaracetam

The company identified 6 RCTs with brivaracetam (N01114, N01193, N01252, N01253, N01254 and N01358), which it included in its indirect comparisons. Of these studies, only study N01254 was potentially relevant for an indirect comparison. The designs of the other studies contained one or several aspects opposed to an inclusion for the benefit assessment. The aspects can be categorized as follows:

- no titration (the dose of brivaracetam was not individually titrated as recommended in the SPC [18])
- study duration too short

Table 5 shows the criteria due to which the respective studies could not be included in the benefit assessment.

Table 5: Reasons for the lack of suitability of the brivaracetam studies included by the company

Study	No titration		Study duration too short
	Dose ≤ 1/2 of maximum dose	Starting dose > SPC	
N01114			●
N01193	●		●
N01252	●		
N01253	●		
N01254			
N01358	●	●	
SPC: Summary of Product Characteristics			

These aspects are described in detail below.

Titration

According to the SPC [18], the recommended starting dose of brivaracetam is 50 mg/day or 100 mg/day, based on the required seizure reduction versus potential side effects. The dose can be adjusted in the dosage range between 50 mg/day and 200 mg/day based on individual patient response and tolerance.

Individual dose adjustment of brivaracetam according to the SPC was conducted only in study N01254. In this study, the dose was blinded and adjusted according to the investigator's assessment during the titration period in a dose range between 20 mg/day and 150 mg/day. The patients in study N01114 were randomly assigned to one of the 3 treatment arms placebo, 50 mg/day brivaracetam and 150 mg/day brivaracetam. Hence the target dose was specified, but the dose was up-titrated in a period of 3 weeks and could be reduced by one step if required. The use of brivaracetam in this study was therefore considered to be in compliance with the approval.

In the studies N01193, N01252, N01253 and N01358, in contrast, the patients were randomly assigned to a fixed dosage of brivaracetam or placebo. Hence in these studies brivaracetam was used without individual titration, either with a starting dose that was too high or without the option for dose escalation. Both approaches were neither meaningful with regard to content nor in compliance with the approval. The extension studies of the brivaracetam studies actually showed that, with flexible dosing, the proportion of patients receiving > 100 mg brivaracetam/day increased in comparison with the main studies. In the studies included by the company, fewer than 30% of the patients received > 100 mg brivaracetam/day, whereas in the extension studies with flexible brivaracetam dose, this number was about 65% [19].

Study duration

With a maintenance phase of 7 weeks without previous titration phase, study N01193 was markedly too short for the derivation of meaningful conclusions for longer treatment. This concurs with the assessment of the European Medicines Agency (EMA), which recommends a duration of the maintenance phase of at least 12 weeks for adjunctive treatment in its guidelines on clinical studies in epilepsy [20]. The maintenance phase in study N01254 was 8 weeks and thus also comparatively short, but there was an additional titration phase of 8 weeks. The dose of the patients was individually titrated so that part of the patients were treated with the individually optimized dose for more than 12 weeks.

Study N01114 also had an additional titration phase. This phase only lasted 3 weeks, however, and the patients did not reach the prespecified dose of brivaracetam before the third week so that in this study the treatment duration with the final dose was notably shorter than 12 weeks. Study N01114 was therefore not relevant for the present benefit assessment because the study duration was too short.

The maintenance phase in each of the studies N01252, N01253 and N01358 was 12 weeks, but the studies were not relevant for the present benefit assessment for other reasons (no titration).

Indirect comparison of brivaracetam versus lacosamide

The company presented an indirect comparison of brivaracetam and lacosamide using the common comparator basic therapy + placebo. This indirect comparison was unsuitable to derive conclusions on the added benefit of brivaracetam versus lacosamide. One of the reasons for this was that the company included brivaracetam studies in this comparison that were unsuitable for the benefit assessment (see above). Another reason was that most of the studies included by the company were not sufficiently similar for an indirect comparison. This also applied to the comparison of the lacosamide studies with the potentially suitable brivaracetam study N01254. Furthermore, the company presented no analyses for several outcomes relevant for the assessment.

Similarity of the study populations

The patient characteristics and further parameters at the start of the study were compared to evaluate the similarity of the study populations. It was shown that the patients in the lacosamide studies partly had more severe disease on average than the patients in the brivaracetam study N01254. This was particularly notable in the frequency of seizures at the start of the study and in the information on pretreatment and disease duration. Table 6 shows the seizure frequency at the start of the study.

Table 6: Seizure frequency

Study	Brivaracetam or lacosamide			Placebo		
	N	Baseline values mean (SD) [median]	Treatment phase values[a] mean (SD) [median]	N	Baseline values mean (SD) [median]	Treatment phase values[a] mean (SD) [median]
Seizure frequency per 28 days						
Study with brivaracetam						
N01254[b, c]	323	20.08 (47.08) [8.8]	15.64 (29.16) [6.8]	108	20.40 (49.92) [9.2]	18.64 (53.04) [7.6]
Studies with lacosamide 400 mg						
EP0008[d]	179	20.70 (28.06) [10.0]	12.77 (18.56) [5.3]	183	26.71 (57.90) [10.5]	24.23 (50.90) [10.3]
SP667[d]	107	26.3 (36.62) [13.0]	21.3 (33.36) [9.0]	96	28.8 (50.34) [11.0]	30.7 (61.07) [10.0]
SP754[d]	201	42.7 (124.78) [11.5]	61.7 (495.96) [7.4]	104	46.9 (109.52) [15.0]	34.6 (67.98) [12.4]
SP755[d]	158	42.0 (203.39) [10.3]	43.9 (273.31) [6.4]	159	21.8 (31.18) [9.9]	20.8 (40.11) [8.0]

a: Treatment phase includes the titration phase and the maintenance phase.
b: Institute's calculation. Recorded in the study documents as seizure frequency per 7 days.
c: Data for the ITT population.
d: Data for the FAS population.
FAS: full analysis set; ITT: intention to treat; N: number of analysed patients; SD: standard deviation

The seizure frequency in the brivaracetam study N01254 at the start of the study was below the frequency in all 4 lacosamide studies (see Table 6). Since some of the patients included in the lacosamide studies had more than 100 seizures/week, this was particularly apparent in the mean seizure frequency (which was apparently largely influenced by individual patients with very high seizure frequency), but also applied to the median seizure frequency. Particularly the patients in the studies SP667 and SP754 apparently had notably more severe disease than the ones in the brivaracetam study N01254.

This finding was supported by the pretreatment and the disease duration of the patients (see Table 7). In the patients in the 2 studies SP667 and SP754, disease duration was longer than in the brivaracetam study, and the number of previous antiepileptic drugs (AEDs) was higher than in the other studies.

Table 7: Number of previous AEDs, disease duration at the start of the study

Study Group	N[a]	Number of prior AEDs % [b]	Duration of disease at the start of the study [years] mean (SD)
Study with brivaracetam			
N01254		**[0-1/2-4/≥ 5]** (5 years before the start of the study)[c]	
BRV 20-150 mg	323[d]	35/54/11	21.8 (12.5)
Placebo	108[d]	34/53/13	22.1 (11.7)
Studies with lacosamide			
EP0008		**[0/1/2/3/≥ 4]** (5 years before the start of the study)[c]	
LCM 400 mg	181	8/19/22/17/34	17.9 (11.7)
Placebo	184	6/14/22/20/38	16.8 (11.5)
SP667		**[1-3/4-6/7+]** (lifelong)[e]	
LCM 400 mg	108	22/30/48	24.7 (13.1)
Placebo	97	15/34/51	24.8 (11.7)
SP754		**[1-3/4-6/7+/missing]** (lifelong)[e]	
LCM 400 mg	204	19/34/45/2	24.4 (13.2)
Placebo	104	14/31/53/2	25.4 (13.3)
SP755		**[1-3/4-6/7+/missing]** (lifelong)[e]	
LCM 400 mg	159	30/31/39/0	22.8 (13.2)
Placebo	163	31/33/35/1	21.3 (12.3)

a: Number of randomized patients. Values that are based on other patient numbers are marked in the corresponding column if the deviation is relevant.
b: Sum > or < 100% possible in the individual study arms due to rounding.
c: Number of AEDs in the last 5 years before the start of the study.
d: Data refer to the patient number for the ITT study population with stratification factor: partial-onset seizures.
e: Number of lifelong AEDs.
AED: antiepileptic drug; BRV: brivaracetam; ITT: intention to treat; LCM: lacosamide; N: number of randomized patients; SD: standard deviation

Missing outcomes

In the category "morbidity", the company presented the outcomes "freedom of seizure" and "50% responder rate" for the assessment of efficacy. Both outcomes are patient-relevant and adequate. They do not provide a complete picture of efficacy, however. Freedom of seizure is only rarely achieved in pharmacoresistant patients as the ones included in the studies. Accordingly, the rates in the studies were low. The change in seizure frequency was therefore considered to be a meaningful supplementation of the 50% responder rate. This outcome was

also mentioned as an important outcome in studies on adjunctive treatment in the EMA guideline on clinical studies in epilepsy [20].

The outcome "seizure frequency" was available for all studies included by the company. The company presented no analyses on this, and provided no justification.

Besides the overall rates of adverse events (AEs), serious AEs (SAEs) and discontinuation due to AEs, the company also analysed specific AEs for the assessment of side effects. The company chose these due to their frequency in the studies (incidence of > 5%) at the Preferred Term (PT) level. The company presented no analysis of AEs at the System Organ Class (SOC) level, although this would have been possible for the company. The analysis of AEs was therefore incomplete. The EMA also mentioned psychiatric disorders such as psychosis, suicidal behaviour/ideation in its assessment of brivaracetam [20].

Indirect comparison of brivaracetam versus eslicarbazepine

The company presented an indirect comparison of brivaracetam and eslicarbazepine using the common comparator basic therapy + placebo. This indirect comparison was unsuitable to derive conclusions on the added benefit of brivaracetam versus eslicarbazepine. One of the reasons for this was that the company included brivaracetam studies in this comparison that were unsuitable for the benefit assessment (see above). Another reason was that most of the eslicarbazepine studies included by the company were also unsuitable for the benefit assessment. In addition, the company did not present analyses on patient-relevant outcomes also in this comparison, although the data were available.

Titration

According to the SPC of eslicarbazepine [21], the recommended starting dose of eslicarbazepine is 400 mg. The dose should be increased to 800 mg after 1 to 2 weeks. Based on individual response, the dose may be increased to 1200 mg. Hence study arms in which patients received an initial dose of 400 mg and, after a titration phase of 1 to 2 weeks, were treated with 800 mg or 1200 mg for at least 12 weeks were relevant for the benefit assessment.

The company did not consider these prerequisites in the inclusion of the studies. Only 4 of the 13 treatment arms included by the company were in compliance with the approval regarding dosage and use of eslicarbazepine (treatment arms with 800 mg and 1200 mg of the BIA-2093-301 study, and the 800 mg treatment arm in each of the studies BIA-2093-303 and BIA-2093-304).

Similarity of the studies

As in the indirect comparison on lacosamide, the patient characteristics and further parameters at the start of the study were compared to evaluate the similarity of the study populations. It was shown in the indirect comparison of brivaracetam versus eslicarbazepine that the patients in the eslicarbazepine studies partly had less severe disease on average than the patients in the

brivaracetam study N01254. Regarding seizure frequency at the start of the study, only the BIA-2093-304 study was in the range of seizure frequency of the brivaracetam study N01254. In the remaining studies with eslicarbazepine, seizure frequency at the start of the study was notably lower. There was no information regarding AED pretreatment of the patients.

Missing outcomes

As in the indirect comparison of brivaracetam versus lacosamide, the company did not present analyses on all patient-relevant outcomes also in the comparison with eslicarbazepine. The outcome "seizure frequency" was available for 4 of the 5 studies included by the company. The company presented no analyses on this, and provided no justification.

Indirect comparison of brivaracetam versus lacosamide/eslicarbazepine

Since both indirect comparisons of brivaracetam versus lacosamide or versus eslicarbazepine were unsuitable, the indirect comparison of brivaracetam versus lacosamide/eslicarbazepine (combined analysis) was also unsuitable to derive conclusions on the added benefit of brivaracetam in comparison with both drugs lacosamide and eslicarbazepine.

2.4 Results on added benefit

The company presented no relevant data for the assessment of the added benefit of brivaracetam in its dossier. This resulted in no hint of an added benefit of brivaracetam in comparison with the ACT; an added benefit is therefore not proven.

2.5 Extent and probability of added benefit

The company presented no suitable data for the assessment of the added benefit of brivaracetam. Hence an added benefit of brivaracetam is not proven for these patients.

The result of the assessment of the added benefit of brivaracetam in comparison with the ACT is summarized in Table 8.

Table 8: Brivaracetam – extent and probability of added benefit

Therapeutic indication	**Appropriate comparator therapy**[a]	**Extent and probability of added benefit**
Adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalization in adult and adolescent (16–18 years) patients with epilepsy	Individual antiepileptic adjunctive treatment, if medically indicated and if no pharmacoresistance/intolerance and contraindications are known yet, with one of the following drugs: eslicarbazepine or gabapentin or lacosamide or lamotrigine or levetiracetam or oxcarbazepine or pregabalin or topiramate or valproic acid or zonisamide	Added benefit not proven
a: Presentation of the appropriate comparator therapy specified by the G-BA. G-BA: Federal Joint Committee		

This deviates from the company's approach, which derived an indication of considerable added benefit of brivaracetam on the basis of the data presented by the company. The added benefit derived by the company was only based on outcomes on side effects.

The G-BA decides on the added benefit.

2.6 List of included studies

Not applicable as no studies were included in the benefit assessment.

References for English extract

Please see full dossier assessment for full reference list.

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