IQWiG Reports – Commission No. A18-48

Brivaracetam (epilepsy in children and adolescents) –

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

Extract

[1] Translation of the executive summary of the dossier assessment *Brivaracetam (Epilepsie bei Kindern und Jugendlichen) – Nutzenbewertung gemäß § 35a SGB V* (Version 1.0; Status: 30 October 2018). Please note: This document was translated by an external translator and 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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Executive summary of the benefit assessment

Background

In accordance with §35a Social Code Book (SBG) 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 is based on a dossier compiled by the pharmaceutical company (hereinafter referred to as the "company"). The dossier was sent to IQWiG on 30 July 2018.

Research question

The aim of this report is to assess the added benefit of brivaracetam as adjunctive therapy for partial seizures with or without secondary generalization in children and adolescents aged ≥ 4 to < 16 years with epilepsy in comparison with the appropriate comparator therapy (ACT).

The ACT specified by the G-BA served as the basis for the research question presented in Table 2 for this benefit assessment.

Table 2[2]: Research questions for the benefit assessment of brivaracetam

Research question	Indication	ACT[a]
1	Adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalization in children and adolescents age ≥ 4 to < 16 years with epilepsy	Individualized adjunctive epilepsy treatment to the extent medically indicated and in the absence of known drug resistance/intolerance or contraindications, using one of the following drugs: Eslicarbazepine[b], gabapentin[b], lacosamide, lamotrigine, levetiracetam, oxcarbazepine[b], topiramate, valproic acid, zonisamide[b] Treatment specified by the physician under consideration of the primary treatment(s) and pretreatment(s) as well as the reason for treatment switch and any adverse events. The respective approval of drugs must be taken into account.
a: Presentation of the ACT specified by the G-BA. b: Approved for children age 6 years and older. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee		

The company followed the G-BA's specification of the ACT.

The assessment was conducted in comparison with the appropriate comparator therapy (ACT) by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. A 12-week minimum duration of maintenance therapy was required.

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

Results

The company included the two studies N01263 and N01266 on brivaracetam in its assessment. The 1-arm N01263 study is unsuitable for assessing the added benefit of brivaracetam since it did not include a maintenance phase, but only a 3-week titration phase. The N01266 study also has a 1-arm design and therefore fails to provide any directly comparative data for a comparison of brivaracetam with the ACT. The company did not present any data on the ACT, thus forgoing any comparisons of individual arms from different studies. However, comparative data would be necessary to assess the benefit. However, there is nothing to suggest that such a comparison would show effects of brivaracetam at a magnitude which is not explicable by systematic bias alone.

Probability and extent of added benefit, patient groups with therapeutically important added benefit[3]

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

The company did not present any suitable data for the assessment of the added benefit of brivaracetam. Consequently, there is no proof of added benefit of brivaracetam in comparison with the ACT.

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

[3] 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, added benefit not proven, or less benefit). For further details see [1,2].

Table 3: Brivaracetam – probability and extent of added benefit

Indication	**ACT[a]**	**Probability and extent of added benefit**
Adjunctive treatment of partial-onset seizures with or without secondary generalization in children and adolescents age ≥ 4 to < 16 years with epilepsy	Individualized adjunctive epilepsy treatment to the extent medically indicated and in the absence of known drug resistance/intolerance or contraindications, using one of the following drugs: Eslicarbazepine[b], gabapentin[b], lacosamide, lamotrigine, levetiracetam, oxcarbazepine[b], topiramate, valproic acid, zonisamide[b] Treatment specified by the physician under consideration of the primary treatment(s) and pretreatment(s) as well as the reason for treatment switch and any adverse events. The respective approval of drugs must be taken into account.	Added benefit not proven
a: Presentation of the ACT specified by the G-BA. b: Approved for children age 6 years and older. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee		

The G-BA decides on the added benefit.

References for English extract

Please see full dossier assessment for full reference list.

1. Institute for Quality and Efficiency in Health Care. General methods: version 5.0 [online]. 10 July 2017 [Accessed: 4 June 2018]. URL: https://www.iqwig.de/download/General-Methods_Version-5-0.pdf.

2. Skipka G, Wieseler B, Kaiser T, Thomas S, Bender R, Windeler J et al. Methodological approach to determine minor, considerable, and major treatment effects in the early benefit assessment of new drugs. Biom J 2015; 58(1): 43-58

The full report (German version) is published under https://www.iqwig.de/en/projects-results/projects/drug-assessment/a18-48-brivaracetam-epilepsy-benefit-assessment-in-accordance-with-35a-social-code-book-v.10444.html.