Gemeinsamer Bundesausschuss

Resolution

of the Federal Joint Committee on an Amendment of the Pharmaceuticals Directive:
Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a (SGB V) and Annex XIIa – Combinations of Medicinal Products with New Active Ingredients according to Section 35a SGB V
Cannabidiol (reassessment of an orphan drug > EUR 30 million turnover limit: seizures associated with tuberous sclerosis, ≥ 2 years)

of 16 May 2024

At its session on 16 May 2024, the Federal Joint Committee (G-BA) resolved to amend the Pharmaceuticals Directive (AM-RL) in the version dated 18 December 2008 / 22 January 2009 (Federal Gazette, BAnz. No. 49a of 31 March 2009), as last amended by the publication of the resolution of D Month YYYY (Federal Gazette, BAnz AT DD.MM.YYYY BX), as follows:

I. Annex XII is amended as follows:

The information on Cannabidiol (seizures associated with tuberous sclerosis, ≥ 2 years, adjunctive therapy) in the version of the resolutions of 4 November 2021 (BAnz AT 17.12.2021 B7) and 5 October 2023 (Banz AT 22.01.2024 B2) is adopted as follows and added after No. 5 to the information on the benefit assessment of cannabidiol in the version of the resolution of 16 May 2024 on the therapeutic indication "Lennox-Gastaut syndrome, ≥ 2 years, combination with clobazam":

Cannabidiol

Resolution of: 16 May 2024
Entry into force on: 16 May 2024
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 16 April 2021):

Epidyolex is indicated for use as adjunctive therapy of seizures associated with tuberous sclerosis (TSC) for patients 2 years of age and older.

Therapeutic indication of the resolution (resolution of 16 May 2024):

See therapeutic indication according to marketing authorisation.

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

Patients 2 years of age and older with seizures associated with tuberous sclerosis

Appropriate comparator therapy for cannabidiol as adjunctive therapy:

- Patient-individual therapy, taking into account the types of seizures occurring, the basic and previous therapy/ therapies and any associated side effects, with selection of

  Brivaracetam, carbamazepine, cenobamate, eslicarbazepine, everolimus, gabapentin, lacosamide, lamotrigine, levetiracetam, oxcarbazepine, perampanel, phenobarbital, phenytoin, pregabalin, topiramate, valproic acid, vigabatrin, zonisamide

Extent and probability of the additional benefit of cannabidiol compared to the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:

Patients 2 years of age and older with seizures associated with tuberous sclerosis

There are no assessable data.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	n.a.	There are no assessable data.
Morbidity	n.a.	There are no assessable data.
Health-related quality of life	n.a.	There are no assessable data.
Side effects	n.a.	There are no assessable data.
Explanations: ↑: statistically significant and relevant positive effect with low/unclear reliability of data ↓: statistically significant and relevant negative effect with low/unclear reliability of data ↑↑: statistically significant and relevant positive effect with high reliability of data ↓↓: statistically significant and relevant negative effect with high reliability of data ↔: no statistically significant or relevant difference ∅: No data available. n.a.: not assessable		

2. Number of patients or demarcation of patient groups eligible for treatment

Patients 2 years of age and older with seizures associated with tuberous sclerosis

Approx. 600 to 2,700 patients

3. Requirements for a quality-assured application

The requirements in the product information are to be taken into account. The European Medicines Agency (EMA) provides the contents of the product information (summary of product characteristics, SmPC) for Epidyolex (active ingredient: cannabidiol) at the following publicly accessible link (last access: 15 April 2024):

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

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

A combination of cannabidiol with other anti-epileptic medicines can lead to pharmacokinetic interactions that can lead to an increase in adverse drug reactions. The patient should be closely monitored for adverse drug reactions. If somnolence or sedation occurs in combination with clobazam, a reduction in the clobazam dosage should be considered.

4. Treatment costs

Annual treatment costs:
Patients 2 years of age and older with seizures associated with tuberous sclerosis

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Cannabidiol	€ 6,563.98 - € 85,769.31
Appropriate comparator therapy:	
Brivaracetam	€ 161.77 - € 1,082.66
Carbamazepine	€ 38.07 - € 266.89[1]
Cenobamate	€ 1,385.57 - € 2,771.13
Eslicarbazepine	€ 616.94 - € 1,965.36
Everolimus	Not calculable
Gabapentin	€ 230.83 - € 993.38
Lacosamide	€ 245.81 - € 472.91[2]
Lamotrigine	€ 138.55 - € 344.80[3]
Levetiracetam	€ 308.30 - € 353.83
Oxcarbazepine	€ 428.50 - € 978.20
Perampanel	€ 338.46 - € 1,240.48[4]
Phenobarbital	€ 332.88 - € 475.01
Phenytoin	Not calculable
Pregabalin	€ 218.05 - € 470.19
Topiramate	€ 244.79 - € 896.22
Valproic acid	€ 73.62 - € 301.93
Vigabatrin Additionally required SHI services	€ 408.45 - € 2,450.72 Not calculable
Zonisamide	€ 954.03 - € 1,721.59

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 April 2024

1 The lowest annual treatment costs result for the minimum maintenance dose in solid dosage form in 2-year-olds. The highest annual treatment costs result for the minimum maintenance dose in liquid dosage form in 2-year-olds. The annual treatment costs of € 184.29 for the maximum maintenance dose in adults are within the range.
2 The lowest annual treatment costs result for the maximum maintenance dose in adults. The highest annual treatment costs result for the minimum maintenance dose in solid dosage form in 2-year-olds.
3 The lowest annual treatment costs result for the minimum maintenance dose in solid dosage form in 2-year-olds. The highest annual treatment costs result for the minimum maintenance dose in liquid dosage form in 2-year-olds. The annual treatment costs of € 262.65 for the maximum maintenance dose in adults are within the range.
4 The lowest annual treatment costs result for the minimum maintenance dose in liquid dosage form in 4-year-olds. The highest annual treatment costs result for the minimum maintenance dose in solid dosage form in 4-year-olds. The annual treatment costs of 1,228.49 for the maximum maintenance dose in adults are within the range.

5. Designation of medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V that can be used in a combination therapy with the assessed medicinal product

In the context of the designation of medicinal products with new active ingredients pursuant to Section 35a, paragraph 3, sentence 4 SGB V, the following findings are made:

Patients 2 years of age and older with seizures associated with tuberous sclerosis

The following medicinal products with new active ingredients that can be used in a combination therapy with cannabidiol in the therapeutic indication of the resolution on the basis of the marketing authorisation under Medicinal Products Act are named (active ingredients and invented names) in accordance with Section 35a, paragraph 3, sentence 4 SGB V:

Brivaracetam (Briviact), cenobamate (Ontozry), vigabatrin (Kigabeq)

The designation of combinations exclusively serves the implementation of the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. The findings made neither restrict the scope of treatment required to fulfil the medical treatment mandate, nor do they make statements about expediency or economic feasibility.

II. **In Annex XIIa of the Pharmaceuticals Directive, the information on cannabidiol (resolution pursuant to Section 35a paragraph 3 SGB V of 4 November 2021) in the therapeutic indication "Epidyolex is indicated for use as adjunctive therapy of seizures associated with tuberous sclerosis (TSC) for patients 2 years of age and older" is adopted as follows:**

"Active ingredient of the assessed medicinal product

Cannabidiol

Resolution according to Section 35a paragraph 3 SGB V from

04.11.2021 and 16.05.2024

Therapeutic indication of the resolution

Epidyolex is indicated for use as adjunctive therapy of seizures associated with tuberous sclerosis (TSC) for patients 2 years of age and older.

Patient group

Patients 2 years of age and older with seizures associated with tuberous sclerosis

Naming of medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V (active ingredients and invented names[2])

Cenobamate (Ontozry), brivaracetam (Briviact), vigabatrin (Kigabeq)

Period of validity of the designation (since... or from... to)

Since 5 October 2023

The designation of combinations exclusively serves the implementation of the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. The findings made neither restrict the scope of treatment required to fulfil the medical treatment mandate, nor do they make statements about expediency or economic feasibility.

III. The resolution will enter into force on the day of its publication on the website of the G-BA on 16 May 2024.

The justification to this resolution will be published on the website of the G-BA at www.g-ba.de.

Berlin, 16 May 2024

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

Prof. Hecken