Gemeinsamer Bundesausschuss

Cannabidiol (reassessment of an orphan drug after exceeding the EUR 30 million turnover limit (Dravet syndrome, ≥ 2 years, combination with clobazam)

Resolution of: 16 May 2024 valid until: unlimited
Entry into force on: 16 May 2024
Federal Gazette, BAnz AT02 07 2024 B3

Therapeutic indication (according to the marketing authorisation of 19 September 2019):

Epidyolex is indicated for use as adjunctive therapy of seizures associated with Lennox-Gastaut syndrome (LGS) or Dravet syndrome (DS), in conjunction with clobazam, for patients 2 years of age and older.

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

Epidyolex is indicated for use as adjunctive therapy of seizures associated with Dravet syndrome (DS) in conjunction with clobazam, for patients 2 years of age and older.

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 Dravet syndrome

Appropriate comparator therapy for cannabidiol in combination with clobazam as adjunctive therapy:

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

  Brivaracetam, bromide, clobazam, fenfluramine, levetiracetam, stiripentol, topiramate, valproic acid

Extent and probability of the additional benefit of cannabidiol in combination with clobazam 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 Dravet syndrome

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 Dravet syndrome

Approx. 500 to 2,900 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 Dravet syndrome

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Cannabidiol	€ 6,563.98 - € 68,265.37
Clobazam	€ 940.32 - € 1,005.65
Total	**€ 7,504.29 - € 69,271.01**
Appropriate comparator therapy:	
Brivaracetam	€ 161.77 - € 1,082.66
Clobazam	€ 940.32 - € 1,005.65
Potassium bromide	€ 3,723.85 - € 16,757.33
Fenfluramine	€ 7,696.55 - € 34,722.21
Additionally required SHI services	€ 36.64
Stiripentol	€ 4,801.45 - € 24,939.23
Topiramate	€ 244.79 - € 896.22
Levetiracetam	€ 308.30 - € 353.83
Valproic acid	€ 73.62 - € 301.93

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

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 Dravet syndrome

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) [indication: only in children aged 2 to < 4 years]

- Period of validity of the designation: 5 October 2023 until 15 May 2024

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

- Period of validity since 16 May 2024

The following medicinal products with new active ingredients that can be used in a combination therapy with the assessed medicinal product in the therapeutic indication of the present resolution on the basis of the marketing authorisation under Medicinal Products Act are excluded from the designation, as the G-BA has identified at least considerable additional benefit for the combination with the assessed medicinal product in the resolution on the benefit assessment of fenfluramine of 15 July 2021 (Federal Gazette, BAnz AT 28.09.2021 B1):

Fenfluramine (Fintempla)

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 15 April 2021) in the therapeutic indication "Epidyolex is indicated for use as adjunctive therapy of seizures associated with Dravet syndrome (DS), in conjunction with clobazam, 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

15.04.2021 and 16.05.2024

Therapeutic indication of the resolution

Epidyolex is indicated for use as adjunctive therapy of seizures associated with […] Dravet syndrome (DS) in conjunction with clobazam, for patients 2 years of age and older.

Patient group

Patients 2 years of age and older with seizures associated with Dravet syndrome

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

Brivaracetam (Briviact) [indication: only in children aged 2 to < 4 years]

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

5 October 2023 until 15 May 2024

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

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

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

Since 16 May 2024

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.