EMA/562057/2022

# European Medicines Agency decision

P/0218/2022

of 8 June 2022

on the acceptance of a modification of an agreed paediatric investigation plan for cannabidiol (Epidyolex), (EMEA-001964-PIP01-16-M04) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

**Disclaimer**

This decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

**Only the English text is authentic.**

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The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0136/2017 issued on 7 June 2017, decision P/0047/2020 issued on 29 January 2020, decision P/0350/2020 issued on 9 September 2020, and decision P/0033/2021 issued on 29 January 2021,

Having regard to the application submitted by GW Pharma (International) B.V. on 18 February 2022 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 20 May 2022, in accordance with Article 22 of Regulation (EC) No 1901/2006,

Having regard to Article 25 of Regulation (EC) No 1901/2006,

Whereas:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the acceptance of changes to the agreed paediatric investigation plan and to the deferral and to the waiver.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, including changes to the deferral and to the waiver.

[1] OJ L 378, 27.12.2006, p.1, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

***Article 1***

Changes to the agreed paediatric investigation plan for cannabidiol (Epidyolex), oral solution, oral use, including changes to the deferral and to the waiver, are hereby accepted in the scope set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices.

***Article 2***

This decision is addressed to GW Pharma (International) B.V., Databankweg 26, 3821 AL – Amersfoort, The Netherlands.

EMA/PDCO/136452/2022
Amsterdam, 20 May 2022

# Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan

EMEA-001964-PIP01-16-M04

## Scope of the application

**Active substance(s):**

Cannabidiol

**Invented name:**

Epidyolex

**Condition(s):**

Treatment of seizures associated with Dravet syndrome

Treatment of seizures associated with Lennox-Gastaut syndrome

Treatment of seizures associated with tuberous sclerosis complex

**Authorised indication(s):**

See Annex II

**Pharmaceutical form(s):**

Oral solution

**Route(s) of administration:**

Oral use

**Name/corporate name of the PIP applicant:**

GW Pharma (International) B.V.

**Information about the authorised medicinal product:**

See Annex II

## Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, GW Pharma (International) B.V. submitted to the European Medicines Agency on 18 February 2022 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/0136/2017 issued on 7 June 2017, decision P/0047/2020 issued on 29 January 2020, decision P/0350/2020 issued on 9 September 2020, and decision P/0033/2021 issued on 29 January 2021.

The application for modification proposed changes to the agreed paediatric investigation plan and to the deferral and to the waiver.

The procedure started on 21 March 2022.

## Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified. The condition Treatment of infantile spasms has been deleted.

## Opinion

1. The Paediatric Committee, having assessed the application in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree to changes to the paediatric investigation plan and to the deferral and to the waiver in the scope set out in the Annex I of this opinion.

   The Paediatric Committee member of Norway agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annexes and appendix.

# Annex I

# The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed paediatric investigation plan (PIP)

# 1. Waiver

## *1.1. Condition*

Treatment of seizures associated with Dravet syndrome (DS)

The waiver applies to:

- the paediatric population from birth to less than 1 year of age;
- oral solution, oral use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s).

## *1.2. Condition*

Treatment of seizures associated with Lennox-Gastaut syndrome (LGS)

The waiver applies to:

- the paediatric population from birth to less than 1 year of age;
- oral solution, oral use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s).

## *1.3. Condition*

Treatment of seizures associated with tuberous sclerosis complex (TSC)

The waiver applies to:

- the paediatric population from birth to less than 1 month of age;
- oral solution, oral use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s).

# 2. Paediatric investigation plan

## *2.1. Condition*

Treatment of seizures associated with Dravet syndrome

### 2.1.1. Indication(s) targeted by the PIP

Treatment of seizures associated with Dravet syndrome

### 2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From 1 year to less than 18 years of age

### 2.1.3. Pharmaceutical form(s)

Oral solution

### 2.1.4. Measures

| Area | Description |
|---|---|
| Quality-related studies | Not applicable. |
| Non-clinical studies | Not applicable. |
| Clinical studies | **Study 1 (GWEP1332)**<br>Randomised double-blind placebo-controlled study to assess the efficacy and safety of cannabidiol, to investigate its pharmacokinetics and its effects on other anti-epileptic drugs in patients with DS.<br>**Study 2 (GWEP1424)**<br>Randomised double-blind placebo-controlled study to assess efficacy and safety of two doses of cannabidiol compared to placebo in patients with DS.<br>**Study 5 (GWEP1415)**<br>Open-label extension study to assess long-term safety of cannabidiol in patients with DS or LGS.<br>**Study 8 (GWEP17006)**<br>*Deleted in procedure EMEA-001964-PIP01-16-M04*.<br>**Study 9 (GWEP17005)**<br>Open label, single-arm study to assess the safety, pharmacokinetics and efficacy of adjunctive cannabidiol in patients with LGS, DS or TSC. |

| | |
|---|---|
| Extrapolation, modelling and simulation studies | **Study 10 (GWPP17025)**<br>A physiological based PK model for cannabidiol (CBD) in a virtual patient population.<br>**Study 11 (GWPP17004)**<br>A joint population PK model for CBD, 7-OH CBD and 7-COOH CBD in healthy adult subjects to re-estimate exposure in PK evaluable patients with Lennox-Gastaut syndrome. |
| Other studies | Not applicable. |
| Other measures | Not applicable. |

## *2.2. Condition*

Treatment of seizures associated with Lennox-Gastaut syndrome

### 2.2.1. Indication(s) targeted by the PIP

Treatment of seizures associated with Lennox-Gastaut syndrome

### 2.2.2. Subset(s) of the paediatric population concerned by the paediatric development

From 1 year to less than 18 years of age

### 2.2.3. Pharmaceutical form(s)

Oral solution

### 2.2.4. Measures

| Area | Description |
|---|---|
| Quality-related studies | Not applicable. |
| Non-clinical studies | Not applicable. |
| Clinical studies | **Study 3 (GWEP1423)**<br>Randomised double-blind placebo-controlled study to assess the efficacy and safety of cannabidiol in patients with LGS.<br>**Study 4 (GWEP1414)**<br>Randomised double-blind placebo-controlled study to assess efficacy and safety of two doses of cannabidiol in patients with LGS.<br>**Study 5 (GWEP1415)**<br>Open-label extension study to assess long-term safety of cannabidiol in patients with DS or LGS (same study as for the condition DS). |

| | |
|---|---|
| | **Study 8 (GWEP17006)**<br>*Deleted in procedure EMEA-001964-PIP01-16-M04*<br>**Study 9 (GWEP17005)**<br>Open label, single-arm study to assess the safety, pharmacokinetics and efficacy of adjunctive cannabidiol in patients with LGS, DS or TSC (same study as for the condition DS). |
| Extrapolation, modelling and simulation studies | **Study 10 (GWPP17025)**<br>A physiological based PK model for CBD in a virtual patient population (same study as for the condition DS).<br>**Study 11 (GWPP17004)**<br>A joint population PK model for CBD, 7-OH CBD and 7-COOH CBD in healthy adult subjects to re-estimate exposure in PK evaluable patients with Lennox-Gastaut syndrome (same study as for the condition DS). |
| Other studies | Not applicable. |
| Other measures | Not applicable. |

## *2.3. Condition*

Treatment of seizures associated with tuberous sclerosis complex

### 2.3.1. Indication(s) targeted by the PIP

Treatment of seizures associated with tuberous sclerosis complex

### 2.3.2. Subset(s) of the paediatric population concerned by the paediatric development

From 1 month to less than 18 years of age

### 2.3.3. Pharmaceutical form(s)

Oral solution

### 2.3.4. Measures

| Area | Description |
|---|---|
| Quality-related studies | Not applicable. |
| Non-clinical studies | Not applicable. |

| | |
|---|---|
| Clinical studies | **Study 6 (GWEP1521)**<br><br>Randomised, placebo-controlled, double-blind parallel-group comparison of two doses of cannabidiol as add-on therapy in patients with TSC, with a one year open-label safety extension.<br><br>**Study 9 (GWEP17005)**<br><br>Open label, single-arm study to assess the safety, pharmacokinetics and efficacy of adjunctive cannabidiol in patients with LGS, DS or TSC (same study as for the condition DS). |
| Extrapolation, modelling and simulation studies | **Study 10 (GWPP17025)**<br><br>A physiological based PK model for CBD in a virtual patient population (same study as for the condition DS).<br><br>**Study 11 (GWPP17004)**<br><br>A joint population PK model for CBD, 7-OH CBD and 7-COOH CBD in healthy adult subjects to re-estimate exposure in PK evaluable patients with Lennox-Gastaut syndrome (same study as for the condition DS). |
| Other studies | Not applicable. |
| Other measures | Not applicable. |

# 3. Follow-up, completion and deferral of PIP

| | |
|---|---|
| Concerns on potential long term safety/efficacy issues in relation to paediatric use: | Yes |
| Date of completion of the paediatric investigation plan: | By January 2025 |
| Deferral for one or more measures contained in the paediatric investigation plan: | Yes |

# Annex II

# Information about the authorised medicinal product

## Condition(s) and authorised indication(s):

1. Treatment of seizures associated with Dravet Syndrome

Authorised indication(s):

- 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.

2. Treatment of seizures associated with Lennox-Gastaut Syndrome

Authorised indication(s):

- Epidyolex is indicated for the treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients 2 years of age and older.

## Authorised pharmaceutical form(s):

Oral solution

## Authorised route(s) of administration:

Oral use