



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

EMA/31950/2021

## European Medicines Agency decision P/0033/2021

of 29 January 2021

on the acceptance of a modification of an agreed paediatric investigation plan for cannabidiol (Epidyolex), (EMEA-001964-PIP01-16-M03) 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<sup>1</sup>,

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

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

Having regard to the application submitted by GW Pharma (International) B.V. on 11 September 2020 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 11 December 2020, 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.
- (2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan.

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<sup>1</sup> OJ L 378, 27.12.2006, p.1.

<sup>2</sup> OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

**Article 1**

Changes to the agreed paediatric investigation plan for cannabidiol (Epidyolex), oral solution, oral use, 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., Databanksweg 26, 3821 AL – Amersfoort, Netherlands.



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

EMA/PDCO/514809/2020 Corr  
Amsterdam, 11 December 2020

## Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan EMA-001964-PIP01-16-M03

### **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 infantile spasms

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 11 September 2020 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, the decision P/0047/2020 issued on 29 January 2020 and the decision P/0350/2020 issued on 9 September 2020.

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

The procedure started on 13 October 2020.

## **Scope of the modification**

Some measures and timelines of the Paediatric Investigation Plan have been modified.

## **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 in the scope set out in the Annex I of this opinion.

The Norwegian Paediatric Committee member 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 6 months 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 6 months 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 infantile spasms (IS)

The waiver applies to:

- the paediatric population from birth to less than 1 month of age and from 25 months to less than 18 years 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).

## 1.4. 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 6 months to less than 18 years of age

#### 2.1.3. Pharmaceutical form(s)

Oral solution

#### 2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	0	Not applicable.
Clinical studies	4	<p><b>Study 1 (GWEP1332)</b></p> <p>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.</p> <p><b>Study 2 (GWEP1424)</b></p> <p>Randomised double-blind placebo-controlled study to assess efficacy and safety of two doses of cannabidiol compared to placebo in patients with DS.</p> <p><b>Study 5 (GWEP1415)</b></p> <p>Open-label extension study to assess long-term safety of cannabidiol in patients with DS or LGS.</p> <p><b>Study 8 (GWEP17006)</b></p> <p>Open label, randomised study to assess the safety, pharmacokinetics and exploratory efficacy of adjunctive cannabidiol as compared with standard of care antiepileptic therapy in patients with DS or LGS.</p>



Extrapolation, modelling and simulation studies	2	<p><b>Study 10 (GWPP17025)</b></p> <p>A physiological based PK model for cannabidiol (CBD) in a virtual patient population.</p> <p><b>Study 11 (GWPP17004)</b></p> <p>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.</p>
Other studies	0	Not applicable.
Other measures	0	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 6 months to less than 18 years of age

### 2.2.3. Pharmaceutical form(s)

Oral solution

### 2.2.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	0	Not applicable.
Clinical studies	4	<p><b>Study 3 (GWEP1423)</b></p> <p>Randomised double-blind placebo-controlled study to assess the efficacy and safety of cannabidiol in patients with LGS.</p> <p><b>Study 4 (GWEP1414)</b></p> <p>Randomised double-blind placebo-controlled study to assess efficacy and safety of two doses of cannabidiol in patients with LGS.</p> <p><b>Study 5 (GWEP1415)</b></p> <p>Open-label extension study to assess long-term safety of cannabidiol</p>

		in patients with DS or LGS (same study as for the condition DS). <b>Study 8 (GWEP17006)</b> Open label, randomised study to assess the safety, pharmacokinetics and exploratory efficacy of adjunctive cannabidiol as compared with standard of care antiepileptic therapy in patients with DS or LGS (same study as for the condition DS).
Extrapolation, modelling and simulation studies	2	<b>Study 10 (GWPP17025)</b> A physiological based PK model for CBD in a virtual patient population (same study as for the condition DS). <b>Study 11 (GWPP17004)</b> 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	0	Not applicable.
Other measures	0	Not applicable.

### 2.3. Condition

Treatment of seizures associated with infantile spasms

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

Treatment of seizures associated with infantile spasms

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

From 1 month to less than 25 months of age

#### 2.3.3. Pharmaceutical form(s)

Oral solution

#### 2.3.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	0	Not applicable.

Clinical studies	1	<p><b>Study 7 (GWEP15100)</b></p> <p>Open-label pilot phase (comprising two sequential cohorts).</p> <p>The placebo-controlled pivotal phase to assess efficacy, safety and pharmacokinetics of cannabidiol was deleted during procedure EMEA-001964-PIP01-16-M03.</p>
Extrapolation, modelling and simulation studies	2	<p><b>Study 10 (GWPP17025)</b></p> <p>A physiological based PK model for CBD in a virtual patient population (same study as for the condition DS).</p> <p><b>Study 11 (GWPP17004)</b></p> <p>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).</p>
Other studies	0	Not applicable.
Other measures	0	Not applicable.

## 2.4. Condition

Treatment of seizures associated with tuberous sclerosis complex

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

Treatment of seizures associated with tuberous sclerosis complex

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

From 1 month to less than 18 years of age

### 2.4.3. Pharmaceutical form(s)

Oral solution

### 2.4.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	0	Not applicable.

Clinical studies	2	<p><b>Study 6 (GWEP1521)</b></p> <p>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.</p> <p><b>Study 9 (GWEP17005)</b></p> <p>Open label, randomised study to assess the safety, pharmacokinetics and exploratory efficacy of adjunctive cannabidiol as compared with standard of care antiepileptic therapy in patients with TSC.</p>
Extrapolation, modelling and simulation studies	2	<p><b>Study 10 (GWPP17025)</b></p> <p>A physiological based PK model for CBD in a virtual patient population (same study as for the condition DS).</p> <p><b>Study 11 (GWPP17004)</b></p> <p>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).</p>
Other studies	0	Not applicable.
Other measures	0	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 2023
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