EMA/312728/2017

European Medicines Agency decision

P/0136/2017

of 7 June 2017

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for cannabidiol (CBD) (EMEA-001964-PIP01-16) 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 Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the application submitted by GW Research Ltd on 18 April 2016 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 21 April 2017, in accordance with Article 18 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation and Article 13 of said Regulation,

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 agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a deferral.

(4) It is therefore appropriate to adopt a decision granting a waiver.

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

Has adopted this decision:

Article 1

A paediatric investigation plan for cannabidiol (CBD), oral solution, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A deferral for cannabidiol (CBD), oral solution, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

A waiver for cannabidiol (CBD), oral solution, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 4

This decision is addressed to GW Research Ltd, Sovereign House, Vision Park, Histon, CB24 9BZ – Cambridge, United Kingdom.

EMA/PDCO/110041/2017 Corr
London, 21 April 2017

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and a waiver

EMEA-001964-PIP01-16

Scope of the application

Active substance(s):

Cannabidiol (CBD)

Condition(s):

Treatment of seizures associated with Dravet Syndrome (DS)

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

Treatment of seizures associated with Infantile Spasms (IS)

Treatment of seizures associated with Tuberous Sclerosis Complex (TSC)

Pharmaceutical form(s):

Oral solution

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

GW Research Ltd

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Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, GW Research Ltd submitted for agreement to the European Medicines Agency on 18 April 2016 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation.

The procedure started on 24 May 2016.

Supplementary information was provided by the applicant on 30 January 2017. The applicant proposed modifications to the paediatric investigation plan and requested a waiver.

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 18 of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation;
   - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(b) of said Regulation, on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified subset(s) of the paediatric population.

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

2. The measures and timelines of the agreed 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 annex 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, for 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, for 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, for 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, for 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 (DS)

2.1.1. Indication(s) targeted by the PIP

Treatment of seizures associated with Dravet Syndrome (DS)

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	**Study 1 (GWEP1332)** 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. **Study 2 (GWEP1424)** Randomised double-blind placebo-controlled study to assess efficacy and safety of two doses of cannabidiol compared to placebo in patients with DS. **Study 5 (GWEP1415)** Open-label extension study to assess long-term safety of cannabidiol in patients with DS or LGS. **Study 8 (GWEP17006)** 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.

Extrapolation, modelling and simulation studies	2	**Study 10 (ID not available yet)** A physiological based PK model for CBD in a virtual patient population. **Study 11 (GWPP17004)** 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	0	Not applicable.
Other measures	0	Not applicable.

2.2. Condition

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

2.2.1. Indication(s) targeted by the PIP

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

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	**Study 3 (GWEP1423)** Randomised double-blind placebo-controlled study to assess the efficacy and safety of cannabidiol in patients with LGS. **Study 4 (GWEP1414)** Randomised double-blind placebo-controlled study to assess efficacy and safety of two doses of cannabidiol in patients with LGS. **Study 5 (GWEP1415)** 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) 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	**Study 10 (ID not available yet)** A physiological based PK model for CBD in a virtual patient population (same study as for the condition DS). **Study 11 (GWPP17004)** 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 (IS)

2.3.1. Indication(s) targeted by the PIP

Treatment of seizures associated with Infantile Spasms (IS)

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	**Study 7 (GWEP15100)** Open-label pilot phase (comprising two sequential cohorts) followed by a randomised double-blind, placebo-controlled pivotal phase to assess efficacy, safety and pharmacokinetics of cannabidiol in patients with IS, with a one year open-label safety extension.
Extrapolation, modelling and simulation studies	2	**Study 10 (ID not available yet)** A physiological based PK model for CBD in a virtual patient population (same study as for the condition DS). Study 11 (GWPP17004) 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.

2.4. Condition

Treatment of seizures associated with Tuberous Sclerosis Complex (TSC)

2.4.1. Indication(s) targeted by the PIP

Treatment of seizures associated with Tuberous Sclerosis Complex (TSC)

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	**Study 6 (GWEP1521)** 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. **Study 9 (GWEP17005)** 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.
Extrapolation, modelling and simulation studies	2	**Study 10 (ID not available yet)** A physiological based PK model for CBD in a virtual patient population (same study as for the condition DS). **Study 11 (GWPP17004)** 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.

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 2022
Deferral for one or more measures contained in the paediatric investigation plan:	Yes