EMA/413448/2020

European Medicines Agency decision

P/0317/2020

of 13 August 2020

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for soticlestat (EMEA-002572-PIP02-19) 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 Takeda Pharma A/S on 25 October 2019 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 26 June 2020, in accordance with Article 17 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 soticlestat, film-coated tablet, age-appropriate oral formulation, oral use, gastric 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 soticlestat, film-coated tablet, age-appropriate oral formulation, oral use, gastric 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 soticlestat, film-coated tablet, age-appropriate oral formulation, oral use, gastric 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 Takeda Pharma A/S, Delta Park 45, 2665 - Vallensbæk Strand, Denmark.

EMA/PDCO/210373/2020
Amsterdam, 26 June 2020

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

EMEA-002572-PIP02-19

Scope of the application

Active substance(s):

Soticlestat

Condition(s):

Treatment of Dravet syndrome

Treatment of Lennox-Gastaut syndrome

Pharmaceutical form(s):

Film-coated tablet

Age-appropriate oral formulation

Route(s) of administration:

Oral use

Gastric use

Name/corporate name of the PIP applicant:

Takeda Pharma A/S

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Takeda Pharma A/S submitted for agreement to the European Medicines Agency on 25 October 2019 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 3 December 2019.

Supplementary information was provided by the applicant on 24 March 2020. The applicant proposed modifications to the paediatric investigation plan.

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 17(1) 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 Dravet syndrome

The waiver applies to:

- Neonates from birth to less than one month of age;
- film-coated tablet and age-appropriate oral formulation, oral use and gastric 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 Lennox-Gastaut syndrome

The waiver applies to:

- Neonates and infants from birth to less than one year of age;
- film-coated tablet and age-appropriate oral formulation, oral use and gastric 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 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 month to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Film-coated tablet and age-appropriate oral formulation

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	2	**Study 1** Development of an age appropriate oral formulation for neonates and children below two years of age *(same study as in PIP EMEA-002572-PIP01-19 and its subsequent modifications)* **Study 2** Study to demonstrate feasibility of administration of the drug product through the G-tube/feeding tube *(same study as in PIP EMEA-002572-PIP01-19 and its subsequent modifications)*
Non-clinical studies	0	Not applicable.
Clinical studies	4	**Study 3** (TAK-935-2002 (OV935)) Multicentre, randomised, double-blind, placebo-controlled study to evaluate the efficacy, safety, and tolerability of soticlestat as an adjunctive therapy in paediatric patients with developmental and/or epileptic encephalopathies (ELEKTRA) **Study 4** (TAK-935-18-001 (OV935)) Open-label extension study to assess the long-term safety, tolerability and effect on seizure frequency of soticlestat as adjunctive therapy in patients with rare epilepsy (ENDYMION) *(same study as in PIP EMEA-002572-PIP01-19 and its subsequent modifications)* **Study 6** (TAK-935-21-bbb (OV935)) Multicentre, randomised, double-blind, placebo-controlled, parallel-group study in paediatric patients from 2 to less than 18 years of age (and adults) with Dravet syndrome (DS), to assess the reduction of convulsive seizure frequency and to assess safety and tolerability of soticlestat **Study 7** (TAK-935-24-ccc (OV935)) Multicentre, open-label, safety, efficacy, and tolerability study of soticlestat in paediatric patients aged from 1 month to less than 2 years with DS
Extrapolation, modelling and simulation studies	1	**Study 9** (TAK-935-24-eee (OV935)) PK/PD, population PK and PBPK modelling to estimate soticlestat exposure parameters in paediatric patients
Other studies	0	Not applicable
Other measures	0	Not applicable

2.2. Condition:

Treatment of 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)

Film-coated tablet and age-appropriate oral formulation

2.2.4. Measures

Area	Number of measures	Description
Quality-related studies	2	**Study 1** Development of an age appropriate oral formulation for neonates and children below two years of age *(Same study as for the condition "Treatment of Dravet syndrome")* **Study 2** Study to demonstrate feasibility of administration of the drug product through the G-tube/feeding tube *(Same study as for the condition "Treatment of Dravet syndrome")*
Non-clinical studies	0	Not applicable.
Clinical studies	4	**Study 3** (TAK-935-2002 (OV935)) Multicentre, randomised, double-blind, placebo-controlled study to evaluate the efficacy, safety, and tolerability of soticlestat as an adjunctive therapy in paediatric patients with developmental and/or epileptic encephalopathies (ELEKTRA) *(Same study as for the condition "Treatment of Dravet syndrome")* **Study 4** (TAK-935-18-001 (OV935)) Open-label extension study to assess the long-term safety, tolerability and effect on seizure frequency of soticlestat as adjunctive therapy in patients with rare epilepsy (ENDYMION) *(Same study as for the condition "Treatment of Dravet syndrome")* **Study 5** (TAK-935-21-aaa (OV935)) Multicentre, randomised, double-blind, placebo-controlled, parallel-group study in paediatric patients from 2 to less than 18 years of age (and adults) with Lennox-Gastaut syndrome

		(LGS), to assess the reduction of drop seizure frequency and to assess safety and tolerability of soticlestat **Study 8** (TAK-935-24-ddd (OV935)) Multicentre, open-label, safety, efficacy, and tolerability study of soticlestat in paediatric patients aged from 1 year to less than 2 years with LGS
Extrapolation, modelling and simulation studies	1	**Study 9** (TAK-935-24-eee (OV935)) PK/PD, population PK and PBPK modelling to estimate soticlestat exposure parameters in paediatric patients *(Same study as for the condition "Treatment of Dravet syndrome")*
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:	No
Date of completion of the paediatric investigation plan:	By December 2026
Deferral for one or more measures contained in the paediatric investigation plan:	Yes