EMA/248085/2024

European Medicines Agency decision

P/0194/2024

of 14 June 2024

on the acceptance of a modification of an agreed paediatric investigation plan for soticlestat, (EMEA-002572-PIP02-19-M05) 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/0317/2020 issued on 13 August 2020, the decision P/0491/2021 issued on 3 December 2021 and the decision P/0251/2023 issued on 14 July 2023,

Having regard to the application submitted by Takeda Pharma A/S on 22 January 2024 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 26 April 2024, 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.

[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 soticlestat, film-coated tablet, age-appropriate oral formulation, oral use, gastric use, intestinal 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 Takeda Pharma A/S, Delta Park 45, 2665 - Vallensbaek Strand, Denmark.

EMA/PDCO/40937/2024
Amsterdam, 26 April 2024

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

EMEA-002572-PIP02-19-M05

Scope of the application

Active substance(s):

Soticlestat

Invented name and authorisation status:

See Annex II

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

Intestinal use

Name/corporate name of the PIP applicant:

Takeda Pharma A/S

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Takeda Pharma A/S submitted to the European Medicines Agency on 22 January 2024 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/0317/2020 issued on 13 August 2020,the decision P/0491/2021 issued on 3 December 2021 and the decision P/0251/2023 issued on 14 July 2023.

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

The procedure started on 26 February 2024.

Scope of the modification

Some measures 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 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 conditions 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 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, gastric and intestinal 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, gastric and intestinal 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	Description
Quality-related studies	**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	Not applicable
Clinical studies	**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-935-3001) 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-XXX) Multicentre, open-label, safety, efficacy, and tolerability study of soticlestat in paediatric patients aged from 1 month to less than 2 years with DS **Study 10** (TAK-935-3003) Open-label extension study to assess the long-term safety and tolerability of soticlestat as adjunctive therapy in patients with Dravet syndrome and Lennox-Gastaut Syndrome *(added in procedure EMEA-002572-MIP01-19-M01)*
Extrapolation, modelling and simulation studies	**Study 9** (TAK-935-24-eee (OV935)) PK/PD, population PK and PBPK modelling to estimate soticlestat exposure parameters in paediatric patients
Other studies	Not applicable
Other measures	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	Description
Quality-related studies	**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	Not applicable
Clinical studies	**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-935-3002) 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-XXX) Multicentre, open-label, safety, efficacy, and tolerability study of soticlestat in paediatric patients aged from 1 year to less than 2 years with LGS. **Study 10** (TAK-935-3003) Open-label extension study to assess the long-term safety and tolerability of soticlestat as adjunctive therapy in patients with Dravet syndrome and Lennox-Gastaut Syndrome *(added in procedure EMEA-002572-MIP01-19-M01)*.
Extrapolation, modelling and simulation studies	**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	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:	No
Date of completion of the paediatric investigation plan:	By June 2028
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

The product is not authorised anywhere in the European Community.