MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

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Decision Cover Letter

Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan (MHRA-100336-PIP01-21-M02) and to the deferral

MHRA-100336-PIP01-21-M03

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; INTESTINAL USE

Name / Corporate name of the PIP applicant

Takeda Pharma A/S

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Takeda Pharma A/S submitted to the licensing authority on 02/09/2024 16:49 BST an application for a Modification

The procedure started on 10/10/2024 12:18 BST

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to accept change(s) to the agreed paediatric investigation plan and to the deferral.

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This decision is forwarded to the applicant, together with its annex and appendix.

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Final Decision Letter

MHRA-100336-PIP01-21-M03

Of 24/10/2024 15:33 BST

On the adopted decision for Soticlestat (MHRA-100336-PIP01-21-M03) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on modification of a paediatric investigation plan (including modification of a waiver or deferral included in that paediatric investigation plan).

This decision applies to a Modification for Soticlestat, Film-coated tablet; Age-appropriate oral formulation , ORAL USE; GASTRIC USE; INTESTINAL USE .

This decision is addressed to Takeda Pharma A/S, Delta Park 45, Vallensbaek Strand, DENMARK, 2665

ANNEX I

1. Waiver

1.1 Condition:

Condition 1: Treatment of Dravet Syndrome. The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 1 month of age. Pharmaceutical form(s): Film-coated tablet Age-appropriate oral formulation Route(s) of administration: ORAL USE GASTRIC USE INTERSTITIAL USE Reason for granting waiver: 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). Condition 2: Treatment of Lennox-Gastaut Syndrome. The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 1 year of age. Pharmaceutical form(s): Film-coated tablet Age-appropriate oral formulation Route(s) of administration: ORAL USE GASTRIC USE INTERSTITIAL USE Reason for granting waiver: 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(s):

Treatment of Dravet Syndrome. Treatment of Lennox-Gastaut Syndrome.

2.2 Indication(s) targeted by the PIP:

Treatment of seizures associated with Dravet Syndrome. Treatment of seizures associated with Lennox-Gastaut Syndrome.

2.3 Subset(s) of the paediatric population concerned by the paediatric development:

Treatment of Dravet Syndrome - The paediatric population from 1 month to less than 18 years of age. Treatment of Lennox-Gastaut Syndrome - The paediatric population from 1 year of age to less than 18 years of age.

2.4 Pharmaceutical Form(s):

Film-coated tablet Age-appropriate oral formulation

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	2	For both conditions: Study 1 Development of an age-appropriate oral formulation for neonates and children below two years of age. Study 2 Study to demonstrate feasibility of administration of the drug product through the G-tube/ feeding tube.
Non-Clinical Studies	0	Not applicable.
Clinical Studies	7	For both conditions: 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). 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. For condition: treatment of Dravet Syndrome: 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. For condition: treatment of Lennox-Gastaut 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 convulsive 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, Modeling & Simulation Studies	1	For both conditions: 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.

3. Follow-up, completion and deferral of a PIP:

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	No

Date of completion of the paediatric investigation plan:	30/06/2028
Deferral of one or more studies contained in the paediatric investigation plan:	Yes