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-100099-PIP01-21- and to the deferral;

MHRA-100099-PIP01-21-M04

Scope of the Application

Active Substance(s)

BRIVARACETAM

Condition(s)

Treatment of paediatric epilepsy syndromes, Treatment of neonatal seizures

Pharmaceutical Form(s)

Oral solution, Solution for injection/infusion, Film-coated tablet

Route(s) of Administration

ORAL USE, INTRAVENOUS, INTRAVENOUS BOLUS

Name / Corporate name of the PIP applicant

UCB Pharma Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, UCB Pharma Limited submitted to the licensing authority on 26/10/2023 16:50 BST an application for a

The procedure started on 15/12/2023 14:43 GMT

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-100099-PIP01-21-M04

Of 05/01/2024 09:41 GMT

On the adopted decision for BRIVARACETAM (MHRA-100099-PIP01-21-M04) 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 for BRIVARACETAM, Oral solution, Solution for injection/infusion, Film-coated tablet , ORAL USE, INTRAVENOUS, INTRAVENOUS BOLUS .

This decision is addressed to UCB Pharma Limited, 208 Bath Road, Slough, Berkshire, Slough, UNITED KINGDOM, SL1 3WE

ANNEX I

1. Waiver

1.1 Condition:

Condition 1: Treatment of paediatric epilepsy syndromes. The waiver applies / applied to: Paediatric Subset(s): Preterm newborn infants, term newborn infants (from birth to less than 28 days of age). Pharmaceutical form(s): Oral solution Film-coated tablet Route(s) of administration: ORAL 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 neonatal seizures. The waiver applies / applied to: Paediatric Subset(s): The paediatric population from 28 days to less than 18 years of age. Pharmaceutical form(s): Oral solution Solution for injection/infusion Route(s) of administration: ORAL USE INTRAVENOUS 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):

Condition 1: Treatment of paediatric epilepsy syndromes. Condition 2: Treatment of neonatal seizures.

2.2 Indication(s) targeted by the PIP:

Condition 1: Treatment of refractory paediatric epilepsy syndromes. Condition 2: Treatment of neonatal seizures with adjunctive administration of brivaracetam.

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

Condition 1: The paediatric population from 28 days to less than 18 years of age. Condition 2: The paediatric population from birth to less than 28 days of age.

2.4 Pharmaceutical Form(s):

Condition 1: Oral solution Film-coated tablet Condition 2: Oral solution Solution for injection/ infusion

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable.
Non-Clinical Studies	3	Study 1 (NCD1671) Nine-week oral toxicity study followed by a 30-day recovery period in juvenile rats. Study 2 (NCD1883) Study to evaluate brain weight in juvenile and adult rats. Study 3 (NCD1863) Nine-month oral toxicity study in juvenile dogs with a 2- month recovery period.
Clinical Studies	6	Study 4 (N01313) In silico study for prediction of brivaracetam disposition in children. Study 5 (N01263) (Same study as in MHRA-100108-PIP01-21-M01 for condition: Treatment of epilepsy with partial onset seizures.) Open label, single arm, multicentre, pharmacokinetic, safety and efficacy study of adjunctive administration of brivaracetam in children aged 1 month to less than 16 years with refractory paediatric epilepsy syndromes or epilepsy.

		Study 6 (N01269) Randomised, dose-finding and confirmatory, double-blind, placebo-controlled, parallel group, multicentre study with a 2-stage adaptive design and randomised withdrawal to evaluate the efficacy, safety and tolerability of brivaracetam as monotherapy. Study 7 deleted during procedure MHRA-100099-PIP01-21-M01. Study 10 (EP0132) added during procedure MHRA-100099-PIP01-21-M01 Open-label, single-arm, multi-centre, long-term follow-up study to evaluate long-term safety, tolerability, and efficacy of brivaracetam. Study 8 (N01331) Modelling and simulation of intravenous brivaracetam pharmacokinetic profiles in children to evaluate dose adaptation rules. Study 9 (N01349) Modified during procedure MHRA-100099-PIP01-21-M02 Open-label study to evaluate safety, pharmacokinetics and activity of brivaracetam (BRV) in neonates with repeated electroencephalographic seizures assessed by video-EEG.
Extrapolation, Modeling & Simulation Studies	0	Not applicable.
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:	Yes
Date of completion of the paediatric investigation plan:	30/06/2025
Deferral of one or more studies contained in the paediatric investigation plan:	Yes