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

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Decision Cover Letter

Decision of the licensing authority to:

agree a paediatric investigation plan and grant a deferral and on the refusal of a waiver

MHRA-100594-PIP01-22

Scope of the Application

Active Substance(s)

N-[4-(6-fluoro-3,4-dihydro-1H-isoquinolin-2-yl)-2,6-dimethyl-phenyl]-3,3-dimethylbutanamide

Condition(s)

Treatment of focal onset seizures

Pharmaceutical Form(s)

Capsule, hard; Age-appropriate oral liquid dosage form Age-appropriate intravenous dosage form

Route(s) of Administration

ORAL USE; INTRAVENOUS USE

Name / Corporate name of the PIP applicant

Xenon Pharmaceuticals Inc.

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Xenon Pharmaceuticals Inc. submitted to the licensing authority on 04/07/2022 11:22 BST an application for a Paediatric Investigation Plan

The procedure started on 16/01/2023 08:10 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 agree a paediatric investigation plan and grant a deferral and refuse a waiver

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-100594-PIP01-22

Of 11/12/2023 18:49 GMT

On the adopted decision for N-[4-(6-fluoro-3,4-dihydro-1H-isoquinolin-2-yl)-2,6-dimethyl-phenyl]-3,3-dimethylbutanamide (MHRA-100594-PIP01-22) 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 a paediatric investigation plan

This decision applies to a Paediatric Investigation Plan for N-[4-(6-fluoro-3,4-dihydro-1H-isoquinolin-2-yl)-2,6-dimethyl-phenyl]-3,3-dimethylbutanamide , Capsule, hard; Age-appropriate oral liquid dosage form Age-appropriate intravenous dosage form , ORAL USE INTRAVENOUS USE .

This decision is addressed to Xenon Pharmaceuticals Inc., 200-3650 Gilmore Way, Burnaby, BC, CANADA, V5G 4W8

ANNEX I

1. Waiver

1.1 Condition:

1.1 Condition: Treatment of focal onset seizures The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth from to less than one month of age. Pharmaceutical form(s): Capsule, hard Age-appropriate oral liquid dosage form Age-appropriate intravenous dosage form Route(s) of administration: ORAL USE INTRAVENOUS USE Reason for granting waiver: Not Applicable Reason for Refusing Waiver: the MHRA disagreed with the applicant(s)' argumentation that the specific medicinal product is likely to be ineffective or unsafe. The waiver request is therefore refused by the MHRA.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of focal onset seizures

2.2 Indication(s) targeted by the PIP:

Treatment of focal onset seizures

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

The paediatric population from birth to less than 18 years of age

2.4 Pharmaceutical Form(s):

Capsule, hard Age-appropriate oral liquid dosage form Age-appropriate intravenous dosage form

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	2	Study 1 (CMC01) Development of an age-appropriate oral reconstitutable liquid dosage form for children from 1 month of age. Study 2 (CMC02) Development of an age-appropriate intravenous dosage form for neonates from birth to 1 month of age.
Non-Clinical Studies	2	Study 3 (NS01) Dose range-finding juvenile toxicity study to evaluate the use of the product in the paediatric population. Study 4 (NS02) Definitive juvenile toxicity study to evaluate the use of the XEN1101 in the paediatric population.
Clinical Studies	4	Study 5 (CX01) Open-label study to evaluate the PK, safety, tolerability and activity of XEN1101 in paediatric patients from 2 years to less than 18 years of age with focal onset seizures (FOS). Study 6 (CX02) Open-label study to evaluate the PK, safety, tolerability and activity of XEN1101 in paediatric patients from 1 month to less than 2 years of age with focal-onset seizures (FOS). Study 7 (CX03) Long-term open-label study to evaluate safety,

		tolerability and activity of XEN1101 in paediatric patients 1 month to less than 18 years of age with focal onset seizures (FOS). Study 8 Open-label parallel group study to evaluate safety, tolerability and efficacy of adjunctive XEN1101 treatment of neonatal seizures in term neonates.
Extrapolation, Modeling & Simulation Studies	3	Study 9 (MS01) Modelling and simulation population PK (popPK) to evaluate the use of XEN1101 in the treatment of focal onset seizures in children from 1 month to less than 18 years of age. Study 10 (MS02) Modelling and simulation physiologically based PK (PBPK) to evaluate the use of XEN1101 in the treatment of focal onset seizures in infants and children from 1 month to less than 2 years of age and in the treatment of neonatal seizures in infants from birth to less than 1 month of age. Extrapolation Plan Studies 4, 5 and 6 are part of an extrapolation plan of efficacy data from adults to the paediatric population from 1 month to less than 18 years of age, as agreed by the Regulatory Agency.
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:	31/01/2030
Deferral of one or more studies contained in the paediatric investigation plan:	Yes