MHRA
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Canary Wharf
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United Kingdom

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Decision Cover Letter

Decision of the licensing authority to:

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

MHRA-101023-PIP01-23-M01

Scope of the Application

Active Substance(s)

ganaxolone

Condition(s)

Treatment of cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder

Pharmaceutical Form(s)

Oral suspension; Age appropriate oral liquid formulation

Route(s) of Administration

ORAL USE

Name / Corporate name of the PIP applicant

Marinus Pharmaceuticals, Inc.

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Marinus Pharmaceuticals, Inc. submitted to the licensing authority on 26/05/2023 22:13 BST an application for a Modification

The procedure started on 09/06/2023 07:11 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-101023-PIP01-23-M01

Of 27/06/2023 15:08 BST

On the adopted decision for ganaxolone (MHRA-101023-PIP01-23-M01) 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 ganaxolone , Oral suspension; Age appropriate oral liquid formulation , ORAL USE .

This decision is addressed to Marinus Pharmaceuticals, Inc., 5 Radnor Corporate Center 100 Matsonford Rd, Suite 500, Radnor, UNITED STATES OF AMERICA, 19087

ANNEX I

1. Waiver

1.1 Condition:

Treatment of cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 6 months of age. Pharmaceutical form(s): Oral suspension Age appropriate oral liquid formulation Route(s) of administration: ORAL USE Reason for granting waiver: on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder

2.2 Indication(s) targeted by the PIP:

Adjunctive treatment of seizures in paediatric patients aged 6 months to less than 18 years old with cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder

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

The paediatric population from 6 months to less than 18 years of age

2.4 Pharmaceutical Form(s):

Oral suspension Age-appropriate oral liquid formulation

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	2	Study 1 Development of a sodium benzoate-free ganaxolone oral suspension (50 mg/mL) appropriate for the paediatric population in the age range from 6 months to less than 18 years. Study 2 Single-arm open label study to assess the palatability of benzoate -free ganaxolone suspension 50 mg/mL in healthy adult subjects (with no ingestion).
Non-Clinical Studies	0	Not applicable.
Clinical Studies	2	Study 3 (1042-CDD-3001) Double-blind, randomised, placebo-controlled add-on efficacy trial followed by a long-term open-label phase of adjunctive ganaxolone treatment for the treatment of primary-type seizures in paediatric patients (and young adults) with genetically confirmed cyclin dependent kinase-like 5 (CDKL5) deficiency disorder (CDD) from 2 years to less than 18 years of age. Study 4 (1042-CDD-3002) Double-blind, randomised, placebo-controlled add-on efficacy trial of adjunctive ganaxolone treatment for the treatment of primary-type seizures in paediatric patients

		with genetically confirmed cyclin dependent kinase-like 5 (CDKL5) deficiency disorder (CDD) from 6 months to less than 2 years of age.
Extrapolation, Modeling & Simulation Studies	1	Study 5 Paediatric population pharmacokinetic (PK/PD) study to enable modelling of the effect of intrinsic and extrinsic factors on the PK and pharmacodynamics of ganaxolone in the paediatric patients from 6 months to less than 18 years.
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:	31/03/2025
Deferral of one or more studies contained in the paediatric investigation plan:	Yes