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 and to the deferral

MHRA-100284-PIP01-21-M02

Scope of the Application

Active Substance(s)

MEXILETINE HYDROCHLORIDE

Condition(s)

Treatment of myotonic disorders

Pharmaceutical Form(s)

Capsule, hard, Oral solution

Route(s) of Administration

ORAL USE GASTRIC USE

Name / Corporate name of the PIP applicant

Lupin Europe GmbH

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Lupin Europe GmbH submitted to the licensing authority on 16/10/2023 16:46 BST an application for a Modification

The procedure started on 19/01/2024 14:44 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-100284-PIP01-21-M02

Of 09/02/2024 07:54 GMT

On the adopted decision for MEXILETINE HYDROCHLORIDE (MHRA-100284-PIP01-21-M02) 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 MEXILETINE HYDROCHLORIDE, Capsule, hard , ORAL USE GASTRIC USE .

This decision is addressed to Lupin Europe GmbH, Hanauer Landstrasse 139-143, Frankfurt, GERMANY, 60314

ANNEX I

1. Waiver

1.1 Condition:

Not applicable.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of myotonic disorders.

2.2 Indication(s) targeted by the PIP:

Symptomatic treatment of myotonic disorders.

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

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of age-appropriate solid formulation (capsule, not containing erythrosine as colourant) in lower strengths appropriate to the paediatric population. Study 2 This study was deleted during procedureMHRA-100284-PIP01-21-M01.
Non-Clinical Studies	1	Study 3 11-week toxicity study in juvenile rats with a 4-week recovery period.
Clinical Studies	3	Study 4 (MEX-NM-301, EudraCT number 2019-003757-28) Open-label, non-comparative study to evaluate the PK, safety and efficacy of mexiletine in children and adolescents 6 years to less than 18 years of age with clinical symptoms or signs of myotonic disorders. Study 5 (MEX-NM-401) Prospective, long-term observational study (registry) of paediatric myotonic disorder patients from birth to less than 6 years of age who are treated with mexiletine Study 7 (MEX-NM-303, EudraCT number 2019-003758-97) Open-label follow-up study evaluating the long-term safety and efficacy of mexiletine in children with myotonic disorders who have completed the initial paediatric studies.
Extrapolation, Modeling & Simulation Studies	1	Study 8 (Modelling and simulation study for dose selection in all paediatric clinical studies) PK

		modelling study to support dosing recommendations in children.
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:	31/01/2025
Deferral of one or more studies contained in the paediatric investigation plan:	Yes