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-100818-PIP01-22-M02

Scope of the Application

Active Substance(s)

BEMPEDOIC ACID

Condition(s)

Treatment of elevated cholesterol

Pharmaceutical Form(s)

Film-coated tablet; Age-appropriate oral liquid formulation; Age-appropriate oral solid formulation

Route(s) of Administration

ORAL USE

Name / Corporate name of the PIP applicant

Esperion Therapeutics, Inc.

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Esperion Therapeutics, Inc. submitted to the licensing authority on 23/01/2024 20:29 GMT an application for a Modification

The procedure started on 14/03/2024 13:22 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-100818-PIP01-22-M02

Of 21/03/2024 15:24 GMT

On the adopted decision for BEMPEDOIC ACID (MHRA-100818-PIP01-22-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 BEMPEDOIC ACID, Film-coated tablet; Age-appropriate oral liquid formulation; Age-appropriate oral solid formulation , ORAL USE .

This decision is addressed to Esperion Therapeutics, Inc., 3891 Ranchero Drive, Suite 150, Ann Arbor, UNITED STATES OF AMERICA, 48108

ANNEX I

1. Waiver

1.1 Condition:

Treatment of elevated cholesterol The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 4 years of age. Pharmaceutical form(s): Film-coated tablet Age-appropriate oral liquid formulation Age-appropriate oral solid 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 elevated cholesterol.

2.2 Indication(s) targeted by the PIP:

Treatment of heterozygous and homozygous familial hypercholesterolemia.

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

The paediatric population from 4 years to less than 18 years of age.

2.4 Pharmaceutical Form(s):

Film-coated tablet Age-appropriate oral liquid formulation Age-appropriate oral solid formulation

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of an age-appropriate formulation.
Non-Clinical Studies	2	Study 2 Dose range-finding juvenile rat toxicity study to evaluate potential adverse effects of bempedoic acid on developing organ systems in juvenile rates beginning on PND 15 until adulthood, and to determine the relevant dose(s) for the definitive juvenile rate study. Study 3 Definitive juvenile rat toxicity study to evaluate potential toxicity of bempedoic acid on developing organ systems in juvenile rats from PND 15 (prepubertal) through sexual maturity to support administration of bempedoic acid to children of at least 4 years of age.
Clinical Studies	3	Study 4 (1002-041) Open-label, un-controlled, dose escalating PK/PD study to evaluate the dose and exposure/response relationship, safety and tolerability of bempedoic acid when added to stable background lipid modifying therapy in patients from 6 years to less than 18 years of age with heterozygous familial hypercholesterolaemia. Study 5 (1002-042) Double-blind, placebo-controlled, parallel-group, efficacy and safety study to

		evaluate the effect of bempedoic acid versus placebo when added to baseline lipid-modifying therapy on percent change from baseline to Week 12 in LDL#C in patients from 6 to less than 18 years of age with heterozygous familial hypercholesterolaemia. Study 6 (1002-051) Open-label, un-controlled, PK/PD, safety and activity study to evaluate the dose and exposure/response relationship, tolerability, safety and activity of bempedoic acid when added to stable background lipid modifying therapy in patients from 4 years to less than 18 years of age with homozygous and compound heterozygous familial hypercholesterolaemia (HoFH and CHeFH).
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:	No
Date of completion of the paediatric investigation plan:	30/09/2027
Deferral of one or more studies contained in the paediatric investigation plan:	Yes