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-100868-PIP01-23-M01) and to the deferral

MHRA-100868-PIP01-23-M02

Scope of the Application

Active Substance(s)

AFAMELANOTIDE

Condition(s)

Treatment of erythropoietic protoporphyria (EPP)

Pharmaceutical Form(s)

Implant Age appropriate prolonged release formulation

Route(s) of Administration

SUBCUTANEOUS USE

Name / Corporate name of the PIP applicant

CLINUVEL (UK) LIMITED

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, CLINUVEL (UK) LIMITED submitted to the licensing authority on 16/04/2024 15:38 BST an application for a Modification

The procedure started on 04/06/2024 13:44 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-100868-PIP01-23-M02

Of 15/07/2024 11:26 BST

On the adopted decision for AFAMELANOTIDE (MHRA-100868-PIP01-23-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 AFAMELANOTIDE, Implant Age appropriate prolonged release formulation , SUBCUTANEOUS USE .

This decision is addressed to CLINUVEL (UK) LIMITED, 6th Floor, 9 Appold Street, London, UNITED KINGDOM, EC2A 2AP

ANNEX I

1. Waiver

1.1 Condition:

Treatment of erythropoietic protoporphyria (EPP) The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 2 years of age Pharmaceutical form(s): Implant Age appropriate prolonged release formulation Route(s) of administration: SUBCUTANEOUS USE Reason for granting waiver: on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of erythropoietic protoporphyria (EPP)

2.2 Indication(s) targeted by the PIP:

Treatment of erythropoietic protoporphyria

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

The paediatric population from 2 years to less than 18 years of age.

2.4 Pharmaceutical Form(s):

Implant; Age appropriate prolonged release formulation

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of age appropriate prolonged release formulation for subcutaneous use.
Non-Clinical Studies	1	Study 2 Juvenile repeat-dose toxicity study in rats followed by 4-week recovery.
Clinical Studies	4	Study 3 Comparative study to evaluate the pharmacokinetics of afamelanotide and the pharmacodynamic response to afamelanotide between subcutaneous administration of solid implant and the age appropriate prolonged release formulation in healthy adults. Study 4 Open-label, multicentre, multiple dose, dose-escalation pharmacokinetic and pharmacodynamic study of afamelanotide age appropriate prolonged release formulation in children from 6 years to less than 18 years with erythropoietic protoporphyria. Study 5 Open-label, multicentre, multiple dose, dose-escalation pharmacokinetic and pharmacodynamic study of afamelanotide age appropriate prolonged release formulation in children from 2 years to less than 6 years with erythropoietic protoporphyria. Study 6 Placebo

		controlled, randomised, double-blind safety, pharmacodynamics and efficacy trial of afamelanotide age appropriate prolonged release formulation in children from 6 years to less than 18 years with erythropoietic protoporphyria, and with an open-label active-only arm in children from 2 years to less than 6 years, with 12 month open-label extension to evaluate safety.
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:	31/03/2028
Deferral of one or more studies contained in the paediatric investigation plan:	Yes