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-101188-PIP01-23-M01

Scope of the Application

Active Substance(s)

fosdenopterin

Condition(s)

Treatment of patients with molybdenum cofactor deficiency (MoCD) Type A

Pharmaceutical Form(s)

Powder for solution for injection

Route(s) of Administration

INTRAVENOUS USE

Name / Corporate name of the PIP applicant

TMC Pharma Services Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, TMC Pharma Services Limited submitted to the licensing authority on 26/09/2023 09:04 BST an application for a Modification

The procedure started on 27/09/2023 10:08 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

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-101188-PIP01-23-M01

Of 12/10/2023 10:01 BST

On the adopted decision for fosdenopterin (MHRA-101188-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 fosdenopterin, Powder for solution for injection , INTRAVENOUS USE .

This decision is addressed to TMC Pharma Services Limited, Lodge Farm Barn, Hartley Wintney, UNITED KINGDOM, RG27 8AS

ANNEX I

1. Waiver

1.1 Condition:

Not applicable

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of molybdenum cofactor deficiency (MoCD) Type A

2.2 Indication(s) targeted by the PIP:

Treatment of patients with molybdenum cofactor deficiency (MoCD) Type A

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):

Powder for solution for injection

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable.
Non-Clinical Studies	2	Study 1 Juvenile toxicity study in rats, for 26-week treatment period and 28-day recovery period. Study 2 Juvenile toxicity study in dogs, for 9-month treatment period and 3- month recovery period.
Clinical Studies	4	Study 3 (ALXN1101-MCD-201) Open-label, multicentre, dose-escalation study to evaluate the safety, activity and pharmacokinetics of fosdenopterin in children with a genetically confirmed diagnosis of Molybdenum cofactor deficiency type A, treated with recombinant Escherichia Coli-derived cyclic pyranopterin monophosphate. Study 4 (ALXN1101-MCD-202) Open-label, multicentre study to evaluate the safety and activity of fosdenopterin in children with a genetic diagnosis of Molybdenum cofactor deficiency type A, or who present with clinical signs and symptoms consistent with Molybdenum cofactor deficiency type A. Study 5 (ALXN1101-MCD-501) Retrospective, observational, noninterventional data collection study to assess safety and efficacy of prior administration of intravenous (IV) recombinant cPMP (rcPMP predecessor of fosdenopterin) in patients with a genetically confirmed diagnosis of

		molybdenum cofactor deficiency (MoCD) type A or who were suspected to have a diagnosis of MoCD type A based on signs and symptoms at the time of rcPMP treatment initiation. Study 6 (ALX-MCD-502) Retrospective and prospective, multinational, multicentre natural history study of molybdenum cofactor and isolated sulfite oxidase deficiencies to characterise the natural history of molybdenum cofactor deficiency (MoCD) type A.
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:	31/08/2021
Deferral of one or more studies contained in the paediatric investigation plan:	No