MHRA
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Canary Wharf
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Decision Cover Letter

Decision of the licensing authority to:

agree a paediatric investigation plan and grant a deferral and grant a waiver

MHRA-101931-PIP01-25

Scope of the Application

Active Substance(s)

bitopertin

Condition(s)

Treatment of erythropoietic protoporphyria, Treatment of X-linked protoporphyria

Pharmaceutical Form(s)

Film-coated tablet; Age-appropriate dosage form

Route(s) of Administration

Oral use

Name / Corporate name of the PIP applicant

DISC MEDICINE, INC.

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, DISC MEDICINE, INC. submitted to the licensing authority on 17/05/2025 00:36 BST an application for a Paediatric Investigation Plan

The procedure started on 06/06/2025 18:28 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 agree a paediatric investigation plan and grant a deferral and grant a waiver

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-101931-PIP01-25

Of 02/02/2026 13:06 GMT

On the adopted decision for bitopertin (MHRA-101931-PIP01-25) 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 a paediatric investigation plan

This decision applies to a Paediatric Investigation Plan for bitopertin, Film-coated tablet; Age-appropriate dosage form , ORAL USE .

This decision is addressed to DISC MEDICINE, INC., 321 Arsenal Street, Suite 101, Watertown, UNITED STATES OF AMERICA, 02472

ANNEX I

1. Waiver

1.1 Condition:

Treatment of erythropoietic protoporphyria The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 1 year of age Pharmaceutical form(s): Film-coated tablet Age-appropriate dosage form 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 as clinical studies(s) are not feasible. 1.2 Condition: Treatment of X-linked protoporphyria The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 1 year of age Pharmaceutical form(s): Film-coated tablet Age-appropriate dosage form 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 as clinical studies(s) are not feasible.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Condition 1: Treatment of erythropoietic protoporphyria; Condition 2: Treatment of X-linked protoporphyria

2.2 Indication(s) targeted by the PIP:

Condition 1: Treatment of erythropoietic protoporphyria; Condition 1: Treatment of X-linked protoporphyria

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

For both conditions: The paediatric population from 1 year to less than 18 years of age

2.4 Pharmaceutical Form(s):

For both conditions: Film-coated tablet; Age-appropriate dosage form

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	2	Study 1 Age-appropriate formulation study to generate quality, oral bioavailability and palatability data to support the suitability of crushing the existing film-coated tablet form. Study 2 Age-appropriate formulation study to develop an alternative dosage form for administration in children not able to swallow the existing film-coated tablets, should the crushed tablets investigated in Study 1 be considered unsuitable.
Non-Clinical Studies	2	Study 3 (1054421) Definitive juvenile rat toxicity study to investigate the effects on development of the juvenile rat following daily administration of bitopertin and to assess the reversibility of observed effects and the potential for effects with delayed onset over a 28-day treatment-free period. Study 4 (2024-011-DISC-1459-R-PK) Lactational transfer study in rats to investigate the potential lactational exposure and tolerability in the offspring following

		oral administration of bitopertin to the lactating female rat.
Clinical Studies	3	Study 5 (DISC-1459-202) Randomised, open#label, parallel#arm trial of bitopertin to evaluate safety, tolerability, efficacy and protoporphyrin IX (PPIX) concentrations in adolescents from 12 years to less than 18 years of age (and adults) with erythropoietic protoporphyria or X-linked protoporphyria. Study 6 (DISC-1459-301) Randomised, double-blind, placebo-controlled, parallel-group study of bitopertin to evaluate the efficacy, safety and tolerability in adolescents from 12 years to less than 18 years of age (and adults) with erythropoietic protoporphyria or X-linked protoporphyria. Study 7 (DISC-1459-401) Open-label, single-treatment-arm study to evaluate the safety, tolerability, preliminary efficacy, pharmacokinetics and pharmacodynamics in paediatric participants from 1 year to less than 12 years of age with erythropoietic protoporphyria or X-linked protoporphyria.
Extrapolation, Modeling & Simulation Studies	3	Study 8 (2024-040-DISC-1459-H-PMX-PBPK) Physiologically Based Pharmacokinetic (PBPK) model to support initial dose selection for planned paediatric clinical study DISC-1459-401 (Study 7). Study 9 Population Pharmacokinetic/Pharmacodynamic (Pop-PK/PD) model to confirm or modify the paediatric dose. Study 10 Extrapolation study to support paediatric efficacy assumptions and confirm PPIX reduction as a clinically meaningful endpoint in Study DISC#1459#401.
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:	31/12/2029
Deferral of one or more studies contained in the paediatric investigation plan:	Yes