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-100247-PIP01-21-M01) and to the deferral

MHRA-100247-PIP01-21-M02

Scope of the Application

Active Substance(s)

BEROTRALSTAT DIHYDROCHLORIDE

Condition(s)

Treatment of hereditary angioedema

Pharmaceutical Form(s)

Capsule, hard, Granules

Route(s) of Administration

ORAL USE

Name / Corporate name of the PIP applicant

BioCryst Ireland Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, BioCryst Ireland Limited submitted to the licensing authority on 05/06/2024 13:26 BST an application for a Modification

The procedure started on 03/09/2024 08:34 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-100247-PIP01-21-M02

Of 08/10/2024 13:00 BST

On the adopted decision for BEROTRALSTAT DIHYDROCHLORIDE (MHRA-100247-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 BEROTRALSTAT DIHYDROCHLORIDE, Capsule, hard, Granules , ORAL USE .

This decision is addressed to BioCryst Ireland Limited, Block 4, Harcourt Centre, Harcourt Road, Dublin, IRELAND, D02HW77

ANNEX I

1. Waiver

1.1 Condition:

Treatment of hereditary angioedema The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 2 years of age Pharmaceutical form(s): Granules Capsule, hard 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 hereditary angioedema

2.2 Indication(s) targeted by the PIP:

Prevention of attacks in patients with hereditary angioedema

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):

Capsule, hard Granules

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 (FORM-01) Development of a multi-particulate dosage form coated to mask the flavour of the drug product for the paediatric population from 2 years to less than 12 years of age.
Non-Clinical Studies	0	Not applicable.
Clinical Studies	3	Study 2 (BCX7353-302, APeX-2) Randomised, double-blind, placebo-controlled, parallel group, 3-parts study to evaluate the efficacy and safety of two dose levels of berotralstat as an oral treatment for the prevention of attacks in paediatric patients from 12 years to less than 18 years of age (and adults) with hereditary angioedema (HAE). Study 3 (BCX7353-204, APeX-S) Open-label study to evaluate the long-term safety of daily oral berotralstat in subjects with Type I and II hereditary angioedema in paediatric patients from 12 years to less than 18 years of age (and adults) with hereditary angioedema (HAE). Study 4 (BCX7353-304) Open label study to evaluate the safety, pharmacokinetics, and effectiveness of berotralstat in paediatric patients from 2 years to less than 12 years of

		age with hereditary angioedema for the prevention of attacks.
Extrapolation, Modeling & Simulation Studies	1	Study 5 (BCX7353-PPK1) Population PK modelling and simulation study to support extrapolation and evaluate the PK of berotralstat in the prevention of attacks in paediatric subjects with HAE from 2 years to less than 12 years of age, to investigate the performance of the intended PK/ PD study designs, and to provide dosing regimens based on adult and adolescent PK and efficacy via simulations.
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:	31/12/2027
Deferral of one or more studies contained in the paediatric investigation plan:	Yes