

**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-100247-PIP01-21-M01

### **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 29/09/2021 02:21 BST an application for a Modification

The procedure started on 07/03/2022 13:12 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-100247-PIP01-21-M01

Of 30/03/2022 17:18 BST

On the adopted decision for BEROTRALSTAT DIHYDROCHLORIDE (MHRA-100247-PIP01-21-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 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
<b>Quality Measures</b>	1	Study 1 Development of a multi-particulate dosage form coated to mask the flavour of the drug product for the paediatric population from 2 to less than 12 years of age (FORM-01).
<b>Non-Clinical Studies</b>	0	Not applicable
<b>Clinical Studies</b>	3	Study 2 Randomized, 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 to less than 18 years of age (and adults) with hereditary angioedema (HAE) (BCX7353-302, APeX-2). Study 3 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 to less than 18 years of age (and adults) with hereditary angioedema (HAE) (BCX7353-204, APeX-S). Study 4 Open label study to evaluate the safety, pharmacokinetics, and effectiveness of berotralstat in paediatric patients from 2 to less than 12 years of age with hereditary angioedema for the prevention of attacks (BCX7353-304).
<b>Extrapolation, Modeling &amp; Simulation Studies</b>	1	Study 5 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 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 (BCX7353-PPK1).
<b>Other Studies</b>	0	Not applicable
<b>Other Measures</b>	0	Not applicable

### 3. Follow-up, completion and deferral of a PIP:

<b>Concerns on potential long term safety and efficacy issues in relation to paediatric use:</b>	No
<b>Date of completion of the paediatric investigation plan:</b>	31/03/2026
<b>Deferral of one or more studies contained in the paediatric investigation plan:</b>	Yes