EMA/148123/2024

European Medicines Agency decision

P/0151/2024

of 6 May 2024

on the acceptance of a modification of an agreed paediatric investigation plan for berotralstat (Orladeyo), (EMEA-002449-PIP02-18-M02) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Disclaimer

This decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

Only the English text is authentic.

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The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0061/2020 issued on 19 February 2020, and the decision P/0353/2021 issued on 8 September 2021,

Having regard to the application submitted by BioCryst Ireland Limited on 18 December 2023 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 22 March 2024, in accordance with Article 22 of Regulation (EC) No 1901/2006,

Having regard to Article 25 of Regulation (EC) No 1901/2006,

Whereas:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the acceptance of changes to the agreed paediatric investigation plan and to the deferral.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, including changes to the deferral.

[1] OJ L 378, 27.12.2006, p.1, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for berotralstat (Orladeyo), capsule, hard, age-appropriate oral solid formulation, oral use, including changes to the deferral, are hereby accepted in the scope set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices.

Article 2

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

EMA/PDCO/12576/2024 Corr[1]
Amsterdam, 22 March 2024

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan

EMEA-002449-PIP02-18-M02

Scope of the application

Active substance(s):

Berotralstat

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of hereditary angioedema

Pharmaceutical form(s):

Capsule, hard

Age-appropriate oral solid formulation

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

BioCryst Ireland Limited

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, BioCryst Ireland Limited submitted to the European Medicines Agency on 18 December 2023 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/0061/2020 issued on 19 February 2020 and the decision P/0353/2021 issued on 8 September 2021.

The application for modification proposed changes to the agreed paediatric investigation plan and to the deferral.

[1] 25 April 2024.

The procedure started on 22 January 2024.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified.

Opinion

1. The Paediatric Committee, having assessed the application in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree to changes to the paediatric investigation plan and to the deferral in the scope set out in the Annex I of this opinion.

   The Paediatric Committee member of Norway agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annexes and appendix.

Annex I

The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed paediatric investigation plan (PIP)

1. Waiver

1.1. Condition:

Treatment of hereditary angioedema

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- capsule, hard, age-appropriate oral solid formulation, oral use;
- 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:

Treatment of hereditary angioedema

2.1.1. Indication(s) targeted by the PIP

Prevention of attacks in patients with hereditary angioedema

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From 2 to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Capsule, hard

Age-appropriate oral solid formulation

2.1.4. Measures

Area	Description
Quality-related studies	**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).
Non-clinical studies	Not applicable
Clinical studies	**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).
Extrapolation, modelling and simulation studies	**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)
Other studies	Not applicable
Other measures	Not applicable

3. Follow-up, completion and deferral of PIP

Concerns on potential long-term safety/efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By December 2027
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

Condition(s) and authorised indication(s)

1. Treatment of angioedema

Authorised indication(s):

- Orladeyo is indicated for routine prevention of recurrent attacks of hereditary angioedema (HAE) in adult and adolescent patients aged 12 years and older.
- Invented name(s): Orladeyo
- Authorised pharmaceutical form(s): Hard capsule (capsule)
- Authorised route(s) of administration: Oral use
- Authorised via centralised procedure