EMA/67983/2020

European Medicines Agency decision

P/0061/2020

of 10 February 2020

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for berotralstat, (EMEA-002449-PIP02-18) 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 Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the application submitted by BioCryst UK on 20 December 2018 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 11 December 2019, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation and Article 13 of said Regulation,

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

Whereas:

(1) The Paediatric Committee of the European Medicines Agency, following a re-examination procedure of the Paediatric Committee's opinion according to Article 25(3) of Regulation (EC) No 1901/2006, has given an opinion on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a deferral.

(4) It is therefore appropriate to adopt a decision granting a waiver.

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

Has adopted this decision:

Article 1

A paediatric investigation plan for berotralstat, capsule, hard, age-appropriate oral solid formulation, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A deferral for berotralstat, capsule, hard, age-appropriate oral solid formulation, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

A waiver for berotralstat, capsule, hard, age-appropriate oral solid formulation, oral us, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 4

This decision is addressed to BioCryst UK, 10 St Pauls Chuchyard 5, EC4M 8AL – London, United Kingdom.

EMA/PDCO/35881/2020
Amsterdam, 31 January 2020

Final opinion of the Paediatric Committee on the agreement of a Paediatric Investigation plan and a deferral and a waiver

EMEA-002449-PIP02-18

Scope of the application

Active substance(s):

Berotralstat

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 UK

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, BioCryst UK submitted for agreement to the European Medicines Agency on 20 December 2018 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

An Opinion was adopted by the Paediatric Committee on 11 December 2019 for the above mentioned product. BioCryst UK received the Paediatric Committee Opinion on 20 December 2019.

On 16 January 2020 BioCryst UK submitted to the European Medicines Agency a written request, including detailed grounds for re-examination of the Opinion.

The re-examination procedure started on 17 January 2020.

Final Opinion

1. The Paediatric Committee, having assessed the detailed grounds for re-examination, in accordance with Article 25(3) of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   1.1. to revise its opinion and

   - to agree the paediatric investigation plan in accordance with Article 17(1) of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation;
   - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

   1.2. following re-examination, to amend the timelines of the paediatric investigation plan and the timelines of the deferral.

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

2. The measures and timelines of the agreed 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 annex 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	Number of measures	Description
Quality-related studies	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)
Non-clinical studies	0	Not applicable
Clinical studies	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

		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** Multicenter, randomized, crossover study to evaluate the safety, pharmacokinetics, and effectiveness of berotralstat in paediatric patients from 2 to less than 18 years of age with hereditary angioedema for the prevention of attacks vs C1 inhibitor (human)
Extrapolation, modelling and simulation studies	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)
Other studies	0	Not applicable
Other measures	0	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 March 2026
Deferral for one or more measures contained in the paediatric investigation plan:	Yes