EMA/469125/2023

European Medicines Agency decision

P/0411/2023

of 25 October 2023

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for deucrictibant (EMEA-003090-PIP02-22) 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 application submitted by Pharvaris Netherlands BV on 17 October 2022 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 8 September 2023, 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 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, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

A paediatric investigation plan for deucrictibant, age-appropriate oral solid dosage form, capsule, soft, tablet, prolonged-release, 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 deucrictibant, age-appropriate oral solid dosage form, capsule, soft, tablet, prolonged-release, 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 deucrictibant, age-appropriate oral solid dosage form, capsule, soft, tablet, prolonged-release, 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 4

This decision is addressed to Pharvaris Netherlands BV, JH Oortweg 21, 2333CH – Leiden, The Netherlands.

EMA/PDCO/273356/2023
Amsterdam, 8 September 2023

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and a waiver

EMEA-003090-PIP02-22

Scope of the application

Active substance(s):

Deucrictibant

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of hereditary angioedema

Pharmaceutical form(s):

Age-appropriate oral solid dosage form

Capsule, soft

Tablet, prolonged-release

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Pharvaris Netherlands BV

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Pharvaris Netherlands BV submitted for agreement to the European Medicines Agency on 17 October 2022 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.

The procedure started on 21 November 2022.

Supplementary information was provided by the applicant on 30 May 2023. The applicant proposed modifications to the paediatric investigation plan.

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - 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.

   The Paediatric Committee member of Norway 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 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, soft; tablet, prolonged-release; age-appropriate oral solid dosage form; 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

Treatment of and prevention of hereditary angioedema (HAE) attacks in paediatric patients from 2 years to less than 18 years of age.

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

From 2 years to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Age-appropriate oral solid dosage form

Capsule, soft

Tablet, prolonged -release

2.1.4. Measures

Area	**Description**
Quality-related studies	**Study 1** Development of oral paediatric immediate-release (IR) and prolonged- release (XR) formulations.
Non-clinical studies	Not applicable
Clinical studies	**Study 2 - PHA-022121 -C306** Double-blind, controlled versus placebo, randomised cross-over study to assess pharmacokinetics, efficacy, and safety study of decucrtibant (PHA-022121) for the treatment of attacks in paediatric patients from 12 years to less than 18

	years of age (and adults) with hereditary angioedema (PHA-022121 -C306). **Study 3 - PHA-022121 -C303 Part B** Single-arm, open label, extension study to assess safety of long-term on-demand treatment of attacks of deucrictibant (PHA-022121) in paediatric patients from 12 years to less than 18 years of age (and adults) with hereditary angioedema (PHA-022121 -C303 Part B). **Study 4 - PHA-022121 -C305** Double-blind, controlled, randomised parallel group study to assess pharmacokinetics, efficacy, and safety study of deucrictibant (PHA-022121) for the prevention of attacks in paediatric patients from 12 years to less than 18 years of age (and adults) with hereditary angioedema (PHA-022121 -C305) **Study 5 - PHA022121-C307** Single-arm, open label, extension study to assess safety of long-term use of deucrictibant (PHA-022121) for the prevention of attacks in paediatric patients from 12 years to less than 18 years of age (and adults) with hereditary angioedema (PHA-022121 t-C307). **Study 6 - PHA022121-pC304** Open-label, sequential two-part study to assess pharmacokinetics, efficacy, and safety of deucrictibant (PHA-022121) for the treatment (Part 1) and prevention (Part 2) of attacks in paediatric patients from 2 years to less than 12 years and adolescents from 12 years to less than 18 years of age weighing less than 40 kg with hereditary angioedema (PHA-022121 -pC304).
Modelling and simulation studies	**Study 7** - **M&S-001** Simulation of plasma concentrations in adolescents (from 12 years to less than 18 years of age) and children (from 2 years to less than 12 years of age) after single and multiple oral administration of the IR and XR formulations of decucrictibant (PHA-022121) and comparison with relevant adult exposure metrics to guide selection of paediatric doses of deucrictibant for the treatment and prevention of hereditary angioedema attacks (M&S-001) **Study 8** - **M&S-002** Modelling and simulation study to confirm selection of the doses for each formulation to be tested in the PIP Study 6 (PHA-022121 - pC304) (M&S-002).

	Study 9 - **M&S-003** PK/PD modelling of data from PIP Study 6 (PHA-022121-pC304) together with the adolescent and adult data per formulation, to support extrapolation of efficacy (M&S-003).
Other studies	Not applicable
Extrapolation plan	Studies 6, 8, and 9 are part of an extrapolation plan covering the paediatric population from 2 years to less than 12 years of age, as agreed by the PDCO.

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 January 2030
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:

The product is not authorised anywhere in the European Community.