EMA/628660/2020

European Medicines Agency decision

P/0501/2020

of 22 December 2020

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for olinciguat (EMEA-002759-PIP01-19) 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 Cyclerion Therapeutics Inc. on 25 March 2020 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 13 November 2020, 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 refusal 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 refusing 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 olinciguat, tablet, age-appropriate oral solid dosage form, 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 olinciguat, tablet, age-appropriate oral solid dosage form, 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 olinciguat, tablet, age-appropriate oral solid dosage form, 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 Cyclerion Therapeutics Inc., 301 Binney Street, 02142 – Cambridge, USA.

EMA/PDCO/488501/2020
Amsterdam, 13 November 2020

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

EMEA-002759-PIP01-19

Scope of the application

Active substance(s):

Olinciguat

Condition(s):

Treatment of sickle cell disease

Pharmaceutical form(s):

Tablet

Age-appropriate oral solid dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Cyclerion Therapeutics Inc.

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Cyclerion Therapeutics Inc. submitted for agreement to the European Medicines Agency on 25 March 2020 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 30 April 2020.

Supplementary information was provided by the applicant on 23 October 2020. 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)(a) of said Regulation, on the grounds that the specific medicinal product is likely to be ineffective or unsafe in part or all of the paediatric population. Article 11(1)(b) of said Regulation, on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified subset(s) of the paediatric population.

   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 Sickle Cell Disease (SCD)

The waiver applies to:

- the paediatric population from birth to less than 6 months;
- tablet, age-appropriate oral solid dosage form, oral use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s);

and

- the paediatric population from 6 months to less than 2 years;
- tablet, age-appropriate oral solid dosage form, oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric investigation plan

2.1. Condition:

Treatment of Sickle Cell Disease (SCD)

2.1.1. Indication(s) targeted by the PIP

Treatment of Sickle Cell Disease (SCD)

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)

Tablet

Age-appropriate oral solid dosage form

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	2	**Study 1 (PED-FORMDEV-1)** Development of several dosage strengths appropriate to the paediatric population **Study 2 (PED-FORMDEV-1)** Development of an age-appropriate oral solid dosage form

Non-clinical studies	2	**Study 3 (JUV-TOX-1)** Dose range-finding juvenile toxicity study **Study 4 (JUV-TOX-2)** Definitive juvenile toxicity study
Clinical studies	3	**Study 5 (OLI-301-PED)** Double-blind, randomised, placebo controlled parallel group study to evaluate the efficacy and acceptability/palatability of olinciguat in children from 12 years to less than 16 years of age with sickle cell disease (SCD) **Study 6 (OLI-301)** Double-blind, randomised, placebo controlled parallel group study to evaluate the efficacy of olinciguat in adolescents from 16 years to less than 18 years of age (and adults) with sickle cell disease **Study 7 (OLI-201-PED)** Open-label, single-arm, sequential dose cohort study to evaluate pharmacokinetics, safety and efficacy of olinciguat in children from 2 years to less than 12 years of age with sickle cell disease
Extrapolation, modelling and simulation studies	1	**Study 8 (POPPK-MOD-UPDATE)** Modelling and simulation study to evaluate the use of olinciguat in children from 2 years to less than 18 years of age with treatment of sickle cell disease
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 August 2028
Deferral for one or more measures contained in the paediatric investigation plan:	Yes