EMA/598798/2020

European Medicines Agency decision

P/0487/2020

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 etrasimod L-arginine (EMEA-002713-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 Arena Pharmaceuticals, Inc. on 14 December 2019 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 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 etrasimod L-arginine, film-coated 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 etrasimod L-arginine, film-coated 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 etrasimod L-arginine, film-coated 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 Arena Pharmaceuticals, Inc., 6154 Nancy Ridge Drive, 92121 - San Diego, United States.

EMA/PDCO/485353/2020
Amsterdam, 13 November 2020

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

EMEA-002713-PIP01-19

Scope of the application

Active substance(s):

Etrasimod L-arginine

Condition(s):

Treatment of ulcerative colitis

Pharmaceutical form(s):

Film-coated tablet

Age-appropriate oral solid dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Arena Pharmaceuticals, Inc.

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Arena Pharmaceuticals, Inc. submitted for agreement to the European Medicines Agency on 14 December 2019 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 28 January 2020.

Supplementary information was provided by the applicant on 7 August 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)(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 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 ulcerative colitis

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- film-coated tablet, 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 ulcerative colitis

2.1.1. Indication(s) targeted by the PIP

Treatment of moderately or severely active ulcerative colitis

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)

Film-coated tablet

Age-appropriate oral solid dosage form

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of an age-appropriate oral solid dosage form
Non-clinical studies	1	**Study 2 (APD334.TOX.009)** Definitive juvenile toxicity study in Sprague Dawley rats.

Area	Number of measures	Description
Clinical studies	4	**Study 3 (APD334-301)** Randomized, double-blind, placebo-controlled study to assess efficacy and safety of etrasimod as compared to placebo in adolescents from 16 years to less than 18 years of age (and adults) with moderately to severely active ulcerative colitis (UC) over a 52 week treatment period. **Study 4 (APD334-302)** Randomized, double-blind, placebo-controlled study to assess efficacy after 12 weeks of treatment and safety of etrasimod as compared to placebo in adolescents from 16 years to less than 18 years of age (and adults) with moderately to severely active ulcerative colitis (UC). **Study 5 (APD334-PED1, APD334-207)** Open-label, single-arm, study to evaluate the efficacy, safety and pharmacokinetics of etrasimod, consisting of a 12-week induction period to evaluate the efficacy, safety and PK and pharmacodynamic (PD) relationship, and a 40-week treatment extension period to evaluate efficacy, PK, and long-term safety of etrasimod in adolescents from 12 years to less than 18 years of age with moderately to severely active ulcerative colitis (UC). **Study 6 (APD334-PED2, APD334-208)** Open-label, single-arm, study to evaluate the efficacy, safety and pharmacokinetics of etrasimod, consisting of a 12-week induction period to evaluate the efficacy, safety and PK and pharmacodynamic (PD) relationship, and a 40-week treatment extension period to evaluate efficacy, PK, and long-term safety of etrasimod in children from 2 years to less than 12 years of age with moderately to severely active ulcerative colitis (UC).
Extrapolation, modelling and simulation studies	2	**Study 7 (MODEL 1)** Population pharmacokinetic model to predict PK exposures and determine appropriate doses in paediatric populations. **Study 8 (MODEL 2)** Population pharmacokinetic/pharmacodynamic model(s) (exposure-response analyses).
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 September 2025
Deferral for one or more measures contained in the paediatric investigation plan:	Yes