EMA/215887/2019

European Medicines Agency decision

P/0157/2019

of 17 April 2019

on the refusal of a modification of an agreed paediatric investigation plan for fevipiprant (EMEA-001315-PIP02-16-M01) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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 European Medicines Agency's decision P/0124/2018 issued on 11 April 2018,

Having regard to the application submitted by Novartis EuroPharm Limited on 23 November 2018 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 1 March 2019, 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 refusal of changes to the agreed paediatric investigation plan.

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

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

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for fevipiprant, tablet, chewable tablet, age-appropriate oral liquid 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, are hereby refused.

Article 2

This decision is addressed to Novartis EuroPharm Limited, Vista Building, Elm Park, Merrion Road, D04 A9N6 – Dublin, Ireland.

EMA/PDCO/836521/2018
London, 1 March 2019

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

EMEA-001315-PIP02-16-M01

Scope of the application

Active substance(s):

Fevipiprant

Condition(s):

Treatment of asthma

Pharmaceutical form(s):

Tablet

Chewable tablet

Age-appropriate oral liquid dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Novartis EuroPharm Limited

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Novartis EuroPharm Limited submitted to the European Medicines Agency on 23 November 2018 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/0124/2018 issued on 11 April 2018.

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

The procedure started on 3 January 2019.

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 refuse the changes proposed by the applicant regarding the paediatric investigation plan.

   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 remain unchanged and are set out in the Annex I.

3. The scientific conclusions and the grounds for refusal are set out in the summary report appended to this opinion.

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 asthma

The waiver applies to:

- the paediatric population from birth to less than 1 year;
- tablet, chewable tablet, age-appropriate oral liquid dosage form, oral use;
- on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).

2. Paediatric investigation plan

2.1. Condition:

Treatment of asthma

2.1.1. Indication(s) targeted by the PIP

Maintenance treatment of uncontrolled persistent asthma in children 1 to less than 18 years old.

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

From 1 to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Tablet

Chewable tablet

Age-appropriate oral liquid dosage form

2.1.4. Measures

Area	**Number of measures**	**Description**
Quality-related studies	2	**Study 1:** Development of a chewable tablet **Study 2:** Development of an age-appropriate oral liquid dosage form

Area	Number of measures	Description
Non-clinical studies	1	**Study 3:** Definitive juvenile toxicity study in Rats
Clinical studies	8	**Study 4** Randomised, double-blind, parallel-group, placebo-controlled study over 52 weeks to assess the efficacy and safety of fevipiprant when added to existing asthma therapy in adolescents (and adults) with uncontrolled severe asthma. (CQAW0039A2307/CQAW039A2314) **Study 5** Bioequivalence/comparative bioavailability to determine the bioavailability study of two different paediatric fevipiprant oral formulations relative to film-coated tablets as well as the relative bioavailability of the two paediatric formulations (CQAW039A2114) **Study 6** Open-label, pharmacokinetic, safety and tolerability study of fevipiprant in paediatric patients aged 6 to <12 years. (CQAW039B2201) **Study 7** Open-label, pharmacokinetic, safety and tolerability study of fevipiprant in paediatric patients aged 1 to <6 years. (CQAW039B2102) **Study 8** Randomised, double-blind, parallel-group, placebo-controlled study to determine efficacy and safety of once daily fevipiprant, compared with placebo in children 6 to <12 years with uncontrolled moderate to severe persistent asthma. (CQAW039B2302) **Study 9** Randomised, double-blind, parallel-group, placebo-controlled study to determine efficacy and safety of once daily fevipiprant, compared with placebo in children 1 to <6 years with uncontrolled moderate to severe persistent asthma. (CQAW039B2301) **Study 10** Randomised, double-blind double-dummy, parallel group study to demonstrate the non-inferiority of once-daily fevipiprant compared with low-dose inhaled corticosteroids (ICS) in children 1 to <6 years with uncontrolled mild persistent asthma. (CQAW039B2304)

Area	Number of measures	Description
		Study 11 Randomised, double-blind double-dummy, parallel group study to demonstrate the non-inferiority of once-daily fevipiprant compared with low-dose inhaled corticosteroids (ICS) in children and adolescents 6 to <18 years with uncontrolled mild persistent asthma. (CQAW039B2305)
Extrapolation, modelling and simulation studies	2	**Study 12** Dose finding population PK modelling and simulation study. **Study 13** Dose finding physiology based PK modelling and simulation study.
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 June 2027
Deferral for one or more measures contained in the paediatric investigation plan:	Yes