EMA/269206/2016

European Medicines Agency decision

P/0131/2016

of 20 May 2016

on the acceptance of a modification of an agreed paediatric investigation plan for vorapaxar (EMEA-000778-PIP02-12-M01) 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.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Contact EMA www.ema.europa.eu/contact

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on the acceptance of a modification of an agreed paediatric investigation plan for vorapaxar (EMEA-000778-PIP02-12-M01) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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/0222/2013 issued on 16 September 2013,

Having regard to the application submitted by Merck Sharp & Dohme (Europe), Inc. on 4 January 2016 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 April 2016, 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 acceptance of changes to the agreed paediatric investigation plan.

(2) It is therefore appropriate to adopt a decision on the acceptance 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 vorapaxar, tablet, solution, oral use, are hereby accepted in the scope set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices.

Article 2

This decision is addressed to Merck Sharp & Dohme (Europe), Inc., Clos du Lynx 5, B-1200 - Brussels, Belgium.

Done at London, 20 May 2016

For the European Medicines Agency
Zaïde Frias
Head of Division
Human Medicines Research and Development Support
(Signature on file)

EMA/PDCO/21220/2016 Corr
London, 1 April 2016

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

EMEA-000778-PIP02-12-M01

Scope of the application

Active substance(s):

Vorapaxar

Condition(s):

Prevention of arterial thromboembolism

Pharmaceutical form(s):

Tablet

Solution

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Merck Sharp & Dohme (Europe), Inc.

Information about the authorised medicinal product:

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Merck Sharp & Dohme (Europe), Inc. submitted to the European Medicines Agency on 4 January 2016 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/0222/2013 issued on 16 September 2013.

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

The procedure started on 2 February 2016.

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Scope of the modification

Some measures of the Paediatric Investigation Plan have been modified.

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 agree to changes to the paediatric investigation plan in the scope set out in the Annex I of this opinion.

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

2. The measures and timelines of the 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: prevention of arterial thromboembolism

The waiver applies to:

- the paediatric population of less than 3 months of age;
- for solution, oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

And

- the paediatric population from birth to less than 18 years of age;
- for tablet, 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: prevention of arterial thromboembolism

2.1.1. Indication(s) targeted by the PIP

Prevention of thromboembolic events in paediatric patients

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

From 3 months to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Solution

2.1.4. Measures

Area	Number of measures	Description
Quality	3	**Measure 1.** Development of age-appropriate oral liquid formulation (solution) **Measure 2.** Demonstration of the adequacy of existing measuring syringes or development of a dedicated measuring syringe and generation of data supporting dosing accuracy across full dose range. **Measure 3.** Open-label, single dose randomized, crossover study to evaluate comparative bioavailability of vorapaxar powder for solution for oral use in healthy subjects

Area	Number of measures	Description
Non-clinical	1	**Measure 4.** Oral toxicity and toxicokinetic study in juvenile rats
Clinical	2	**Measure 5.** In vitro platelet aggregation study with vorapaxar in paediatric (3 months to less than 18 years) and adult platelets **Measure 6.** Randomized, open-label, multicentre study to evaluate efficacy, safety and tolerability of vorapaxar versus investigative site standard of care in the prophylaxis of thrombotic complications in infants and toddlers from 3 months of age, children and adolescents with cardiac malformations
Extrapolation, modelling and simulation studies	0	Not applicable.
Other studies	0	Not applicable.
Other measures	0	Not applicable.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety and issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By June 2022
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Prevention of arterial thromboembolism

Authorised indication(s):

Zontivity, co-administered with acetylsalicylic acid (ASA) and, where appropriate, clopidogrel, is indicated for the reduction of atherothrombotic events in adult patients with a history of myocardial infarction (MI).

Authorised pharmaceutical form(s):

Film-coated tablet.

Authorised route(s) of administration:

Oral use