EMA/267765/2020

European Medicines Agency decision

P/0199/2020

of 20 May 2020

on the acceptance of a modification of an agreed paediatric investigation plan for apixaban (Eliquis), (EMEA-000183-PIP02-12-M03) 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 European Medicines Agency's decision P/0013/2013 issued on 23 January 2013, the decision P/0235/2013 issued on 24 September 2013 and the decision P/0153/2018 issued on 25 May 2018,

Having regard to the application submitted by Bristol-Myers Squibb / Pfizer EEIG on 27 January 2020 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 30 April 2020, 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 and to the deferral.

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

[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 apixaban (Eliquis), film-coated tablet, age-appropriate oral liquid dosage form, age-appropriate dosage form, other, oral use, including changes to the deferral, 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 covers all conditions, indications, pharmaceutical forms, routes of administration, measures, timelines, waivers and deferrals, as agreed in the decision P/8/2009 issued on 27 January 2009, including subsequent modifications thereof.

Article 3

This decision is addressed to Bristol-Myers Squibb / Pfizer EEIG Plaza 254 - Blanchardstown Corporate Park 2 D15 T867 - Dublin 15, Ireland.

EMA/PDCO/66803/2020
Amsterdam, 30 April 2020

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

EMEA-000183-PIP02-12-M03

Scope of the application

Active substance(s):

Apixaban

Invented name:

Eliquis

Condition(s):

Treatment of venous thromboembolism

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Film-coated tablet

Age-appropriate oral liquid dosage form

Age-appropriate dosage form, other

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Bristol-Myers Squibb / Pfizer EEIG

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Bristol-Myers Squibb / Pfizer EEIG submitted to the European Medicines Agency on 27 January 2020 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0013/2013 issued on 23 January 2013, the decision P/0235/2013 issued on 24 September 2013 and the decision P/0153/2018 issued on 25 May 2018.

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

The procedure started on 2 March 2020.

Scope of the modification

Some measures and timelines 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 and to the deferral 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 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

Not applicable

2. Paediatric Investigation Plan

2.1. Condition:

Treatment of venous thromboembolism

2.1.1. Indication(s) targeted by the PIP

Treatment of venous thromboembolism

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

From birth to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Film-coated tablet for oral use.

Age-appropriate oral liquid dosage form

Age-appropriate dosage form, other

2.1.4. Measures

Area	**Number of studies**	**Description**
Quality-related studies	0	Not applicable
Non-clinical studies	0	Not applicable
Clinical studies	1	**Study 1** Open-label, multi-centre, randomized, active controlled trial to provide PK data and data on anti-Xa activity to support the extrapolation of efficacy to children, to evaluate safety and efficacy of apixaban in children (full term neonates of at least 2.6 kg to less than 18 years of age) who require anticoagulation for a venous thromboembolism.
Extrapolation, modelling and simulation studies	1	**Study 2** (added during modification M03) Modelling and simulation study to derive dosing of apixaban for use in neonates for treatment of venous thromboembolism.
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:	Yes
Date of completion of the paediatric investigation plan:	By April 2024
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 venous thromboembolism

   Authorised indication(s):

   - Prevention of venous thromboembolic events in patients who have undergone elective hip or knee replacement surgery.

2. Prevention of arterial thromboembolism

   Authorised indication(s):

   - Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (NVAF), with one or more risk factors, such as prior stroke or transient ischaemic attack (TIA); age ≥75 years; hypertension; diabetes mellitus; symptomatic heart failure (NYHA Class ≥II).

3. Treatment of venous thromboembolism

   Authorised indication(s):

   - Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults (see section 4.4 for haemodynamically unstable PE patients).

Authorised pharmaceutical formulation(s):

Film-coated tablet

Authorised route(s) of administration:

Oral use