EMA/393010/2013

European Medicines Agency decision

P/0163/2013

of 29 July 2013

on the acceptance of a modification of an agreed paediatric investigation plan for rivaroxaban (Xarelto), (EMEA-000430-PIP01-08-M04) 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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on the acceptance of a modification of an agreed paediatric investigation plan for rivaroxaban (Xarelto), (EMEA-000430-PIP01-08-M04) 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/223/2009 issued on 4 November 2009, the decision P/95/2010 issued on 2 June 2010, the decision P/171/2011 issued on 8 July 2011, and the decision P/0134/2012 issued on 6 July 2012,

Having regard to the application submitted by Bayer Pharma AG on 22 March 2013 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 14 June 2013, 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 rivaroxaban (Xarelto), age-appropriate liquid formulation, film-coated tablet, 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 Bayer Pharma AG, D-13342 – Berlin, Germany.

Done at London, 29 July 2013

For the European Medicines Agency
Guido Rasi
Executive Director
(Signature on file)

EMA/PDCO/203332/2013

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

EMEA-000430-PIP01-08-M04

Scope of the application

Active substance(s):

Rivaroxaban

Invented name:

Xarelto

Condition(s):

Prevention of thromboembolic events

Treatment of thromboembolic events

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Age-appropriate liquid formulation

Film-coated tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Bayer Pharma AG

Information about the authorised medicinal product:

See Annex II

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Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Bayer Pharma AG submitted to the European Medicines Agency on 22 March 2013 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/223/2009 issued on 4 November 2009, the decision P/95/2010 issued on 2 June 2010, the decision P/171/2011 issued on 8 July 2011, and the decision P/0134/2012 issued on 6 July 2012.

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

The procedure started on 15 April 2013.

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 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.

London, 14 June 2013

On behalf of the Paediatric Committee
Dr Daniel Brasseur, Chairman
(Signature on file)

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

1. Waiver

1.1. Condition: prevention of thromboembolic events

The waiver applies to:

- all subsets of the paediatric population from birth to less than 18 years of age;
- for age-appropriate liquid formulation and film-coated tablet, 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).

2. Paediatric Investigation Plan

2.1. Condition: treatment of thromboembolic events

2.1.1. Indication(s) targeted by the PIP

Treatment (secondary prevention) 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)

- Age-appropriate liquid formulation for oral use;
- Film-coated tablet oral use.

2.1.4. Measures

Area	Number of studies	Description
Quality	1	Measure 1: Age-appropriate liquid formulation for oral use
Non-clinical	2	Measure 2: Toxicology study in juvenile rats with a treatment duration of three weeks Measure 3: Toxicology study in juvenile rats with a treatment duration of thirteen weeks
Clinical	5	Measure 4: Relative bioavailability and food effect of oral suspension in healthy adults Measure 5: Multicentre, open-label, non-controlled, single dose study to evaluate safety, tolerability, pharmacokinetics and pharmacodynamics of rivaroxaban in children from 6 months to less than 18 years of age who have been treated for venous thromboembolism

		Measure 6: Multicentre, open-label, active-controlled, randomized, multiple dose study to evaluate safety and PK/PD of rivaroxaban film-coated tablets and oral suspension in paediatric patients from 6 years to less than 18 years of age who have been pre-treated for at least two months with either low molecular weight heparin and/or vitamin K antagonist for venous thromboembolism Measure 7: Multicentre, open-label, active-controlled, randomized, multiple dose study to evaluate safety and PK/PD of rivaroxaban oral suspension in paediatric patients from 6 months to less than 6 years of age who have been pre-treated for at least two months with either low molecular weight heparin and/or vitamin K antagonist for venous thromboembolism Measure 8: Multicentre, open-label, active-controlled, randomized, multiple dose study to evaluate safety and efficacy of rivaroxaban oral suspension and film-coated tablets in paediatric patients from birth to less than 18 years of age who have acute venous thromboembolism

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety or efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By February 2019
Deferral for one or more studies contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Prevention of thromboembolic events

   Authorised indications:

   - Prevention of venous thromboembolism (VTE) in adult patients undergoing elective hip or knee replacement surgery.
   - Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation with one or more risk factors, such as congestive heart failure, hypertension, age => 75 years, diabetes mellitus, prior stroke or transient ischaemic attack.

2. Treatment of thromboembolic events

   Authorised indications:

   - Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation with one or more risk factors, such as congestive heart failure, hypertension, age => 75 years, diabetes mellitus, prior stroke or transient ischaemic attack.
   - Treatment of deep vein thrombosis (DVT), and prevention of recurrent DVT and pulmonary embolism (PE) following an acute DVT in adults.

Authorised pharmaceutical form(s):

Film-coated tablet

Authorised route(s) of administration:

Oral use