EMA/309268/2010

European Medicines Agency decision

P/95/2010

of 2 June 2010

on the acceptance of a modification of an agreed paediatric investigation plan for rivaroxaban (Xarelto) (EMEA-000430-PIP01-08-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.

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on the acceptance of a modification of an agreed paediatric investigation plan for rivaroxaban (Xarelto) (EMEA-000430-PIP01-08-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/223/2009 issued on 4 November 2009,

Having regard to the application submitted by Bayer Schering Pharma AG on 5 February 2010 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 16 April 2010, 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.

(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 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 Schering Pharma AG, 13342 Berlin, Germany.

Done at London, 2 June 2010

For the European Medicines Agency
Thomas Lönngren
Executive Director

(Signature on file)

EMA/PDCO/225029/2010

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

EMEA-000430-PIP01-08-M01

Scope of the application

Active substance(s):

Rivaroxaban

Invented name:

Xarelto

Condition(s):

Venous thromboembolism

Pharmaceutical form(s):

Age-appropriate formulation

Film coated tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Bayer Schering Pharma AG

Information about the authorised medicinal product: see Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Bayer Schering Pharma AG submitted to the European Medicines Agency on 5 February 2010 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 of 4 November 2009. The application for modification proposed changes.

The procedure started on 18 February 2010.

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Scope of the modification

Some measures and timelines of the original Opinion 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 proposed by the applicant regarding the measures and the timelines of the paediatric investigation plan,

   The Icelandic and the Norwegian Paediatric Committee members agree 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, 16 April 2010

On behalf of the Paediatric Committee
Dr Daniel Brasseur, Chairman

(Signature on file)

Annex I

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

1. Condition(s)

Venous thromboembolism

2. Waiver

- Proposed PIP indications
  - Prevention of venous thromboembolism in hospitalised medically ill patients
  - Prevention of stroke and non-central nervous system embolism in subjects with non-valvular atrial fibrillation
  - Prevention of venous thromboembolism in adult patients undergoing elective hip and knee replacement surgery
  - Prevention of atherothrombotic events in patients with a recent acute coronary syndrome

The waiver applies to:

- All subsets of the paediatric population from birth to less than 18 years of age.
- for age-appropriate 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).

3. Paediatric Investigation Plan

3.1. Condition to be investigated

Venous thromboembolism

3.1.1. Indication targeted by the PIP

Treatment and secondary prevention of venous thromboembolism

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

From birth to less than 18 years of age.

3.1.3. Pharmaceutical form(s)

- Age-appropriate formulation for oral use
- Film coated tablet: 1.25 mg, 2.5 mg, 5 mg, 10 mg, 15 mg, 20 mg and 30 mg for oral use

3.1.4. Studies

Area	Number of studies	Description
Quality	1	• Age appropriate formulation for oral use
Non-clinical	2	• Non - Clinical Study 1: Toxicologic study in juvenile rats with a treatment duration of three weeks • Non - Clinical Study 2: Toxicologic study in juvenile rats with a treatment duration of thirteen weeks
Clinical	5	• Clinical Study 1: Relative bioavailability and food effect of age-appropriate formulation in healthy adults • Clinical Study 2: Safety, tolerability, pharmacokinetic, and pharmacodynamic study of rivaroxaban • Clinical Study 3: four week multinational, multicenter, open-label, active-controlled, randomized, multiple dose, prospective study to evaluate safety and PK/PD of rivaroxaban film coated tablets in paediatric subjects 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. • Clinical Study 4: four week multinational, multicenter, open-label, active-controlled, randomized, multiple dose, prospective study to evaluate safety and PK/PD of rivaroxaban age-appropriate formulation in paediatric subjects 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 antagonis for venous thromboembolism. • Clinical Study 5: three months multinational, multicenter, open-label, active-controlled, randomized, multiple dose, prospective study to evaluate safety and efficacy of rivaroxaban age-appropriate formulation and film coated tablets in paediatric subjects from birth to less than 18 years of age who have acute venous thromboembolism

4. Follow-up, completion and deferral of PIP

Measures to address long term follow-up of potential safety issues in relation to paediatric use:	**No**
Date of completion of the paediatric investigation plan:	By October 2017
Deferral for one or more studies contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

EU Number	Invented name Name	Strength	Pharmaceutical form	Route of administration	Packaging	Package size
EU/1/08/472/001	Xarelto	10 mg	Film-coated tablet	Oral use	blister (PVC/PVDC/alu)	5 tablets
EU/1/08/472/002	Xarelto	10 mg	Film-coated tablet	Oral use	blister (PVC/PVDC/alu)	10 tablets
EU/1/08/472/003	Xarelto	10 mg	Film-coated tablet	Oral use	blister (PVC/PVDC/alu)	30 tablets
EU/1/08/472/004	Xarelto	10 mg	Film-coated tablet	Oral use	blister (PVC/PVDC/alu)	100 tablets
EU/1/08/472/005	Xarelto	10 mg	Film-coated tablet	Oral use	blister (PP/alu)	5 tablets
EU/1/08/472/006	Xarelto	10 mg	Film-coated tablet	Oral use	blister (PP/alu)	10 tablets
EU/1/08/472/007	Xarelto	10 mg	Film-coated tablet	Oral use	blister (PP/alu)	30 tablets
EU/1/08/472/008	Xarelto	10 mg	Film-coated tablet	Oral use	blister (PP/alu)	100 tablets