European Medicines Agency

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EUROPEAN MEDICINES AGENCY DECISION

of 27 November 2009

on the acceptance of a modification of an agreed Paediatric Investigation Plan for Dabigatran etexilate mesilate (Pradaxa) (EMEA-000081-PIP01-07-M01) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council as amended

(ONLY THE ENGLISH TEXT IS AUTHENTIC)

DISCLAIMER: This Decision does not entitle to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006, as amended.

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THE EUROPEAN MEDICINES AGENCY,

Having regard to the Treaty establishing the European Community,

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 as amended 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 decision P/76/2008 of the European Medicines Agency on 14 September 2008,

Having regard to the application submitted by Boehringer Ingelheim International GmbH on 10 September 2009 under Article 22 of Regulation (EC) No 1901/2006 as amended proposing changes to the agreed Paediatric Investigation Plan,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 13 November 2009, in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended,

Having regard to Article 25 of Regulation (EC) No 1901/2006 as amended,

WHEREAS:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the acceptance of changes to an agreed Paediatric Investigation Plan,

(2) It is therefore appropriate to adopt a Decision on the acceptance of changes to an 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 Dabigatran etexilate mesilate (Pradaxa), capsule, hard and age-appropriate formulation, 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 accepted.

Article 2

This decision, that supersedes previous decision of the European Medicines Agency P/76/2008, as far as the agreed changes to the PIP for Dabigatran etexilate mesilate (Pradaxa) are concerned, is addressed to Boehringer Ingelheim International GmbH, Binger Straße 173, 55216 Ingelheim am Rhein, Germany.

Done at London, 27 November 2009

For the European Medicines Agency
Thomas Lönngren
Executive Director

(Signature on file)

European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

Doc. Ref. EMEA/PDCO/691639/2009
EMEA-000081-PIP01-07-M01

OPINION OF THE PAEDIATRIC COMMITTEE ON THE ACCEPTANCE OF A MODIFICATION OF AN AGREED PAEDIATRIC INVESTIGATION PLAN

Scope of the application

Active substance(s):
Dabigatran etexilate mesilate

Invented name:
Pradaxa

Condition(s):
Prevention of thromboembolic events
Treatment of thromboembolic events

Pharmaceutical form(s):
Capsule, hard
Age-appropriate formulation

Route(s) of administration:
Oral use

Name/corporate name of the PIP applicant:
Boehringer Ingelheim International GmbH

Information about the authorised medicinal product:
See Annex I

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Boehringer Ingelheim International GmbH submitted to the EMEA on 10 September 2009 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the EMEA decision P/76/2008 of 14 September 2008. The application for modification proposed changes.

The procedure started on 15 October 2009.

Scope of the modification

The modifications concerned details and timelines of the clinical trials.

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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 the changes proposed by the applicant regarding the measures and the timelines of the paediatric investigation plan.

The Icelandic and the Norwegian Paediatric Committee members 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 Agency, together with its annex(es) and appendix.

London, 13 November 2009

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

A. CONDITION(S) / DISEASE(S)

Prevention of thromboembolic events
Treatment of thromboembolic events

B. WAIVER

- **Condition**

Primary venous thrombotic event prevention

  - **Subset(s) of the paediatric population, pharmaceutical form(s) and route(s) of administration covered**

    The waiver applies to: children aged 0 years to less than 18 years for the hard capsule and the age-appropriate formulation, for oral use.

- **Condition**

Thromboembolic event prevention in atrial fibrillation

  - **Subset(s) of the paediatric population, pharmaceutical form(s) and route(s) of administration covered**

    The waiver applies to: children aged 0 years to less than 18 years for the hard capsule and the age-appropriate formulation, for oral use.

C. PAEDIATRIC INVESTIGATION PLAN

C.1. Condition to be investigated

Venous thrombotic event treatment (secondary venous thrombotic event prevention)

- **Proposed PIP indication**

Treatment of venous thromboembolic events in paediatric patients

- **Subset(s) covered**

Children from birth to less than 18 years

- **Formulation(s)**

Age-appropriate formulation

- **Studies / Measures**

Area	Number of studies	Description
Clinical	7	(1) Relative bioavailability study of the paediatric and adult formulations (2) Open-label pharmacokinetic and safety study of dabigatran etexilate mesilate given for 3 days at the end of standard anticoagulant therapy in children aged 12 years to less than 18 years (3) Open-label pharmacokinetic and safety study of dabigatran etexilate mesilate given for 3 days at the end of standard anticoagulant therapy in successive groups of children aged 2 years to less than 12 years, and 1 year to less than 2 years (4) Open-label, randomized, active-controlled, PK/PD and safety study of dabigatran etexilate mesilate versus enoxaparin used for 20 days in children aged 12 years to less than 18 years, 2 years to less than 12 years, and 1 year to less than 2 years (5) Open-label, randomized, active-controlled, PK/PD and safety study of dabigatran etexilate mesilate versus enoxaparin used for 20 days in children aged less than 1 year (6) Open-label, randomised, active-controlled, multi-centre non-inferiority study of dabigatran etexilate mesilate versus enoxaparin for 3 months on the complete thrombus resolution, recurrence of a venous thrombotic event and development of the pro-thrombotic syndrome in children aged 0 years to less than 18 years (7) Open-label, single-arm safety study of dabigatran etexilate for extended secondary prevention of venous thrombosis in children aged 0 years to less than 18 years

Measures to address long term follow-up of potential safety issues in relation to paediatric use:	**Yes**
Date of completion of the paediatric investigation plan:	**By June 2017**
Deferral for some or all studies contained in the paediatric investigation plan:	**Yes**

ANNEX II

INFORMATION ABOUT THE AUTHORISED MEDICINAL PRODUCT

EU Number	Invented name	Strength	Pharmaceutical Form	Route of Administration	Packaging	Content (concentration)	Package size
EU/1/08/442/001	Pradaxa	75 mg	Capsule, hard	Oral use	blister (alu/alu)		10 x 1 capsules
EU/1/08/442/002	Pradaxa	75 mg	Capsule, hard	Oral use	blister (alu/alu)		30 x 1 capsules
EU/1/08/442/003	Pradaxa	75 mg	Capsule, hard	Oral use	blister (alu/alu)		60 x 1 capsules
EU/1/08/442/004	Pradaxa	75 mg	Capsule, hard	Oral use	bottle (PP)		60 capsules
EU/1/08/442/005	Pradaxa	110 mg	Capsule, hard	Oral use	blister (alu/alu)		10 x 1 capsules
EU/1/08/442/006	Pradaxa	110 mg	Capsule, hard	Oral use	blister (alu/alu)		30 x 1 capsules
EU/1/08/442/007	Pradaxa	110 mg	Capsule, hard	Oral use	blister (alu/alu)		60 x 1 capsules
EU/1/08/442/008	Pradaxa	110 mg	Capsule, hard	Oral use	bottle (PP)		60 capsules