EMA/398370/2010

European Medicines Agency decision

P/107/2010

of 28 June 2010

on the acceptance of a modification of an agreed paediatric investigation plan for dabigatran etexilate mesilate (Pradaxa)(EMEA-000081-PIP01-07-M02) 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/76/2008 issued on 14 September 2008 and the decision P/246/2009 issued on 27 November 2009,

Having regard to the application submitted by Boehringer Ingelheim International GmbH on 31 March 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 11 June 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 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 dabigatran etexilate mesilate (Pradaxa), capsule, hard, age-appropriate formulation, 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 Boehringer Ingelheim International GmbH, Binger Straße 173, 55216 Ingelheim am Rhein, Germany.

Done at London, 28 June 2010

For the European Medicines Agency
Thomas Lönngren
Executive Director

(Signature on file)

EMA/PDCO/346222/2010

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

EMEA-000081-PIP01-07-M02

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 II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Boehringer Ingelheim International GmbH submitted to the European Medicines Agency on 31 March 2010 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the

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European Medicines Agency's decision P/246/2009 issued on 27 November 2009, the decision P/76/2008 issued on 14 September 2008.

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

The procedure started on 15 April 2010.

Scope of the modification

Some 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 to the paediatric investigation plan in the scope set out in the Annex I of this opinion,

   The Norwegian Paediatric Committee member(s) 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, 11 June 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)

Prevention of thromboembolic events

Treatment of thromboembolic events

2. Waiver

2.1. 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.

2.2. 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.

3. Paediatric Investigation Plan

3.1. Condition to be investigated

Venous thrombotic event treatment (secondary venous thrombotic event prevention)

3.1.1. Indication targeted by the PIP

Treatment of venous thromboembolic events in paediatric patients

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

Children from birth to less than 18 years

3.1.3. Pharmaceutical form(s)

Age-appropriate formulation

3.1.4. Studies

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

4. Follow-up, completion and deferral of PIP

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	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