



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/503627/2011

European Medicines Agency decision P/175/2011

of 4 July 2011

on the acceptance of a modification of an agreed paediatric investigation plan for dabigatran etexilate mesilate (Pradaxa) (EMA-000081-PIP01-07-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 726/2004¹,

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 Agency²,

Having regard to the European Medicines Agency's decision P/76/2008 issued on 14 September 2008, the decision P/246/2009 issued on 27 November 2009 and the decision P/107/2010 issued on 28 June 2010,

Having regard to the application submitted by Boehringer Ingelheim International GmbH on 1 April 2011 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 17 June 2011, 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 dabigatran etexilate mesilate (Pradaxa), capsule, hard, age-appropriate formulation, 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 is addressed to Boehringer Ingelheim International GmbH, Binger Straße 173, 55216 Ingelheim am Rhein, Germany.

Done at London, 4 July 2011

For the European Medicines Agency
Andreas Pott
Acting Executive Director
(Signature on file)



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/PDCO/421295/2011

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan EMA-000081-PIP01-07-M03

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 1 April 2011 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/76/2008 issued on 14 September 2008, the decision P/246/2009 issued on 27 November 2009, and the decision P/107/2010 issued on 28 June 2010.

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

The procedure started on 20 April 2011.

A meeting with the Paediatric Committee took place on 15 June 2011.

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 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 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, 17 June 2011

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. Waiver

1.1. Condition: Prevention of thromboembolic events

- The waiver applies to: the paediatric population from birth to less than 18 years for the hard capsule and the age-appropriate formulation, for oral use.

2. Paediatric Investigation Plan

2.1. Condition: Treatment of thromboembolic events

2.1.1. Indication targeted by the PIP

Treatment of venous thromboembolic events in paediatric patients (secondary venous thrombotic event prevention).

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

Children from birth to less than 18 years.

2.1.3. Pharmaceutical form(s)

Age-appropriate formulation.

2.1.4. Studies

Area	Number of studies	Description
Quality	1	Study 1: Development of an age-appropriate formulation.
Non-clinical	0	Not applicable.
Clinical	7	Study 2: Relative bioavailability study of the paediatric and adult formulations. Study 3: 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. Study 4: 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. Study 5: 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. Study 6: 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. Study 7: 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 from birth to less than 18 years. Study 8: Open-label, single-arm safety study of dabigatran etexilate for extended secondary prevention of venous thrombosis in children from birth to less than 18 years.

3. 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

Condition(s) and authorised indication(s):

1. Prevention of thromboembolic events

Authorised indications:

- Primary prevention of venous thromboembolic events in adult patients who have undergone elective total hip replacement surgery or total knee replacement surgery.

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