EMA/812162/2018

European Medicines Agency decision

P/0399/2018

of 7 December 2018

on the acceptance of a modification of an agreed paediatric investigation plan for dabigatran etexilate mesilate (Pradaxa) (EMEA-000081-PIP01-07-M11) 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.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Contact EMA www.ema.europa.eu/contact

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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, the decision P/246/2009 issued on 27 November 2009, the decision P/107/2010 issued on 28 June 2010, the decision P/175/2011 issued on 4 July 2011, the decision P/0033/2012 issued on 3 February 2012, the decision P/0228/2012 issued on 1 October 2012, the decision P/0007/2014 issued on 22 January 2014, the decision P/0241/2014 issued on 29 September 2014, the decision P/0057/2016 issued on 18 March 2016 and the decision P/0282/2016 issued on 4 November 2016 and the decision P/0301/2017 issued on 6 October 2017.

Having regard to the application submitted by Boehringer Ingelheim International GmbH on 16 July 2018 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 19 October 2018, 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.

EMA/PDCO/497614/2018 Corr
London, 19 October 2018

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

EMEA-000081-PIP01-07-M11

Scope of the application

Active substance(s):

Dabigatran etexilate mesilate

Invented name:

Pradaxa

Condition(s):

Prevention of thromboembolic events

Treatment of thromboembolic events

Authorised indication(s):

See Annex II

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

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

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 16 July 2018 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, the decision P/107/2010 issued on 28 June 2010, the decision P/175/2011 issued on 4 July 2011, the decision P/0033/2012 issued on 3 February 2012, the decision P/0228/2012 issued on 1 October 2012, the decision P/0007/2014 issued on 22 January 2014, the decision P/0241/2014 issued on 29 September 2014, the decision P/0057/2016 issued on 18 March 2016 and the decision P/0282/2016 issued on 4 November 2016 and the decision P/0301/2017 issued on 6 October 2017.

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

The procedure started on 21 August 2018.

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 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.

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 (PIP)

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;
- capsule, hard, age-appropriate formulation, oral use;
- on the grounds that clinical studies cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the paediatric population.

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)

Capsule, hard

Age-appropriate formulation

2.1.4. Measures

Area	Number of studies	Description
Quality	1	**Study 1** Development of an age-appropriate formulation
Non-clinical	0	Not applicable
Clinical	6	**Study 2** Relative bioavailability study of the paediatric and adult formulations

		Study 3 Open-label trial to evaluate pharmacokinetics and safety of dabigatran etexilate in children aged 12 years to less than 18 years **Study 4** Open-label, single-dose trial to evaluate pharmacokinetics, pharmacodynamics, safety and tolerability of dabigatran etexilate in children aged 1 year to less than 12 years Study 6: Open-label, single-dose study to evaluate pharmacokinetics, pharmacodynamics, tolerability and safety of dabigatran etexilate in children aged less than 1 year **Study 7** Open-label, randomised, active-controlled, multi-centre, non-inferiority study to evaluate efficacy and safety of dabigatran etexilate versus standard of care in children from birth to less than 18 years **Study 8** Open-label, single-arm, long-term study to evaluate the safety of dabigatran etexilate in children from birth to less than 18 years
Extrapolation, modelling and simulation studies	0	Not applicable
Other studies	0	Not applicable
Other measures	0	Not applicable

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By April 2019
Deferral for some or all measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

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

Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (NVAF), with one or more risk factors, such as prior stroke or transient ischemic attack (TIA); age ≥ 75 years; heart failure (NYHA Class ≥ II); diabetes mellitus; hypertension.

Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults.

Authorised pharmaceutical form(s):

Capsule, hard

Authorised route(s) of administration:

Oral use