EMA/235549/2014

European Medicines Agency decision

P/0112/2014

of 5 May 2014

on the agreement of a paediatric investigation plan and on the refusal of a waiver for enalapril (maleate) (EMEA-001516-PIP01-13) 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 application submitted by Pharmathen S.A. on 8 July 2013 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 21 March 2014, in accordance with Article 18 of Regulation (EC) No 1901/2006, and Article 13 of said Regulation,

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 agreement of a paediatric investigation plan and on the refusal of a waiver.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision refusing a waiver.

[1] OJ L 378, 27.12.2006, p.1.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

A paediatric investigation plan for enalapril (maleate), tablet for oral suspension, orodispersible film, 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, is hereby agreed.

Article 2

A waiver for enalapril (maleate), tablet for oral suspension, orodispersible film, 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, is hereby refused.

Article 3

This decision is addressed to Pharmathen S.A., 6 Dervenakion str, 15351 - Pallini, Greece.

Done at London, 5 May 2014

For the European Medicines Agency
Guido Rasi
Executive Director
(Signature on file)

EMA/PDCO/49390/2014 Corr

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and on the refusal of a waiver

EMEA-001516-PIP01-13

Scope of the application

Active substance(s):

Enalapril (maleate)

Condition(s):

Treatment of hypertension

Pharmaceutical form(s):

Tablet for oral suspension

Orodispersible film

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Pharmathen S.A.

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Pharmathen S.A. submitted for agreement to the European Medicines Agency on 8 July 2013 an application for a paediatric investigation plan for the above mentioned medicinal product.

The procedure started on 15 August 2013.

Supplementary information was provided by the applicant on 19 December 2013. The applicant proposed modifications to the paediatric investigation plan and requested a waiver.

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Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 18 of said Regulation;
   - to refuse the granting of a waiver in accordance with Article 13 of said Regulation, for some of the subsets of the paediatric population and the above mentioned condition(s) as it does not meet the grounds detailed in Article 11(1) of said Regulation.

   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 agreed 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 annex and appendix.

London, 21 March 2014

On behalf of the Paediatric Committee
Dr Dirk Mentzer, Chairman
(Signature on file)

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

1. Waiver

1.1. Condition: treatment of hypertension

The request for the waiver applied to:

- preterm and term newborn infants from birth to less than one month of age;
- for tablet for oral suspension and for orodispersible film, for oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

The waiver request does not provide evidence to support the following grounds set out in Article 11(1) of Regulation (EC) No 1901/2006 that:

- (a) the specific medicinal product is likely to be ineffective or unsafe in the paediatric population;

Because:

- the PDCO disagreed with the applicant(s)' argumentation that the specific medicinal product is likely to be ineffective or unsafe.

The waiver request is therefore refused by the PDCO.

2. Paediatric Investigation Plan

2.1. Condition: treatment of hypertension

2.1.1. Indication(s) targeted by the PIP

Treatment of hypertension.

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

From birth to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Tablet for oral suspension

Orodispersible film

2.1.4. Measures

Area	Number of studies	Description
Quality	2	**Study 1:** Development of an orodispersible film of enalapril for children from 1 to less than 18 years of age with hypertension. **Study 2:** Development of a tablet for oral suspension of enalapril for children from birth to less than 18 years of age with hypertension.
Non-clinical	0	Not applicable.
Clinical	1	**Study 3:** Open-label study to explore the plasma pharmacokinetic parameters, the safety and the efficacy of enalapril after single and multiple dose in hypertensive children from birth to less than 6 years of age.
Other	1	**Study 4:** Extrapolation of the pharmacodynamics of enalapril from adults to children using a PKPD model.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety or efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By February 2018
Deferral for one or more measures contained in the paediatric investigation plan:	No