EMA/468294/2014

European Medicines Agency decision

P/0219/2014

of 3 September 2014

on the acceptance of a modification of an agreed paediatric investigation plan for enalapril (maleate) (EMEA-001241-PIP02-13-M01) 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/0050/2014 issued on 7 March 2014,

Having regard to the application submitted by Proveca Limited on 28 April 2014 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 18 July 2014, 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 enalapril (maleate), oral solution, 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 Proveca Limited, Daresbury Innovation Centre, Keckwick Lane, Daresbury, WA4 4FS – Halton, United Kingdom.

Done at London, 3 September 2014

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

EMA/PDCO/271257/2014

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

EMEA-001241-PIP02-13-M01

Scope of the application

Active substance(s):

Enalapril (maleate)

Condition(s):

Treatment of heart failure

Pharmaceutical form(s):

Oral solution

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Proveca Limited

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Proveca Limited submitted to the European Medicines Agency on 28 April 2014 an application for modification of the agreed paediatric investigation plan as set out in the European Medicines Agency's decision P/0050/2014 issued on 7 March 2014.

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

The procedure started on 21 May 2014.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified.

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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 changes to the paediatric investigation plan 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 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, 18 July 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

Not applicable.

2. Paediatric Investigation Plan

2.1. Condition: treatment of heart failure

2.1.1. Indication(s) targeted by the PIP

Treatment of heart failure

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)

Oral solution for oral use.

2.1.4. Measures

Area	Number of measures	Description
Quality	3	**Study 1:** Development of an enalapril-containing formulation suitable for administration via the oral route to the paediatric population from birth to less than 18 years of age (PRO/ENA/004) **Study 2:** An adult trained taste panel to assess the palatability of the enalapril oral formulation prior to its use in children (PRO/ENA/005) **Study 3:** Assessment of the in vitro stability of enalapril in the new formulation in combination with milk feed and simulated "gastric juices of an infant" plus in vitro assessment of parenteral feeding as used with nasogastric/gastronomy tubes in older children (PRO/GLY/ENA/007)
Non-clinical	0	Not applicable.
Clinical	4	**Study 4:** Bioequivalence / comparative bioavailability study in adult healthy volunteers comparing the new liquid formulation of enalapril with a licensed enalapril tablet (PRO/ENA/006)

Area	Number of measures	Description
		Study 5: Open label, single dose population pharmacokinetic study of oral enalapril administered to children from birth to less than 12 years of age, diagnosed with heart failure secondary to both high and low output disease (PRO/ENA/001) **Study 6:** Open label, 12 month safety study in children from birth to less than 12 months of age at entry to study receiving enalapril for heart failure (PRO/ENA/002) **Study 7:** Systematic literature review, data extrapolation and modeling (PRO/ENA/003)

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 March 2018
Deferral for one or more measures contained in the paediatric investigation plan:	No