EMA/628700/2020

European Medicines Agency decision

P/0507/2020

of 22 December 2020

on the acceptance of a modification of an agreed paediatric investigation plan for captopril (EMEA-001544-PIP01-13-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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on the acceptance of a modification of an agreed paediatric investigation plan for captopril (EMEA-001544-PIP01-13-M02) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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/0206/2014 issued on 8 August 2014,

Having regard to the application submitted by Proveca Pharma Limited on 31 July 2020 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 13 November 2020, 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 captopril, age-appropriate oral liquid dosage form, 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 Pharma Limited, Marine House, Clanwilliam Place, Dublin 2 - Dublin, Ireland.

EMA/PDCO/440545/2020
Amsterdam, 13 November 2020

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

EMEA-001544-PIP01-13-M02

Scope of the application

Active substance(s):

Captopril

Condition(s):

Treatment of heart failure

Pharmaceutical form(s):

Age-appropriate oral liquid dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Proveca Pharma Limited

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Proveca Pharma Limited submitted to the European Medicines Agency on 31 July 2020 an application for modification of the agreed paediatric investigation plan as set out in the European Medicines Agency's decision P/0206/2014 issued on 8 August 2014.

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

The procedure started on 15 September 2020.

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 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

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)

Age-appropriate oral liquid dosage form

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	2	**Study 1 (PRO/CAP/003)** Development of an age-appropriate captopril oral solution **Study 2 (PRO/CAP/004)** In vitro stability study of the developed age-appropriate captopril oral solution
Non-clinical studies	0	Not applicable
Clinical studies	4	**Study 3 (PRO/CAP/005)** Study to investigate the palatability of the developed (in Study 1) age-appropriate captopril oral solution in an adult population **Study 4 (PRO/CAP/006)** Bioequivalence study in adult healthy volunteers to compare the developed (in Study 1) age-appropriate captopril oral solution with a licensed captopril tablet **Study 5 (PRO/CAP/001)** Open-label, single dose population PK study of oral captopril administered to children from birth to less than 12 years of age, diagnosed with heart failure

		Study 6 (PRO/CAP/007) - Study deleted during procedure EMEA-001544-PIP01-13-M02 **Study 8 (PRO/CAP/008) - Study added during procedure EMEA-001544-PIP01-13-M02** Retrospective cohort safety study of captopril administered for prevention or treatment of heart failure in paediatric patients from birth to 1 year of age
Extrapolation, modelling and simulation studies	1	**Study 7 (PRO/CAP/002)** Systematic literature review of the available evidence in adolescents and extrapolation/modelling to support a paediatric application for captopril in the treatment of heart failure
Other studies	0	Not applicable
Other measures	0	Not applicable

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By June 2025
Deferral for one or more measures contained in the paediatric investigation plan:	No

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Treatment of hypertension

Authorised indication(s):

- Captopril is indicated for the treatment of essential hypertension.

2. Treatment of heart failure

Authorised indication(s):

- Captopril is indicated for the treatment of chronic heart failure.

3. Treatment of myocardial infarction

Authorised indication(s):

- Captopril is indicated in any clinically stable patient within the first 24 hours of an infraction.
- Captopril is indicated in clinically stable patients with asymptomatic left ventricular dysfunction.

4. Treatment of treatment of diabetic nephropathy

Authorised indication(s):

- Captopril is indicated for the treatment of macroproteinuric diabetic nephropathy in patients with type I diabetes.

Authorised pharmaceutical form(s):

- Oral solution
- Tablets

Authorised route(s) of administration:

Oral use