EMA/617360/2015

European Medicines Agency decision

P/0240/2015

of 30 October 2015

on the acceptance of a modification of an agreed paediatric investigation plan for sacubitril / valsartan (LCZ696) (EMEA-000316-PIP02-11-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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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/0096/2012 issued on 30 May 2012, and the decision P/0106/2014 issued on 5 May 2014,

Having regard to the application submitted by Novartis Europharm Ltd. on 22 June 2015 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and proposing a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 11 September 2015, in accordance with Article 22 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 acceptance of changes to the agreed paediatric investigation plan and on the granting of a waiver.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision on the granting of 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

Changes to the agreed paediatric investigation plan for sacubitril / valsartan (LCZ696), film-coated tablet, age-appropriate solid oral 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

A waiver for sacubitril / valsartan (LCZ696), film-coated tablet, age-appropriate solid oral dosage form, oral use, the details of which are set out in the opinion of the Paediatric Committee the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

This decision is addressed to Novartis Europharm Ltd., Frimley Business Park, GU16 7SR – Camberley United Kingdom.

Done at London, 30 October 2015

For the European Medicines Agency
Zaïde Frias
Head of Division
Human Medicines Research and Development Support
(Signature on file)

EMA/PDCO/436302/2015
London, 11 September 2015

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

EMEA-000316-PIP02-11-M02

Scope of the application

Active substance(s):

Sacubitril / valsartan (LCZ696)

Condition(s):

Treatment of heart failure

Pharmaceutical form(s):

Film-coated tablet

Age-appropriate solid oral dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Novartis Europharm Ltd.

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Novartis Europharm Ltd. submitted to the European Medicines Agency on 22 June 2015 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0096/2012 issued on 30 May 2012, and the decision P/0106/2014 issued on 5 May 2014.

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

The procedure started on 14 July 2015.

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Scope of the modification

Some measures of the Paediatric Investigation Plan have been modified. A waiver for a new paediatric subset has been added.

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;
   - to grant a waiver for one or more subsets of the paediatric population concluded in accordance with Article 11(1)(a) of said Regulation, on the grounds that the specific medicinal product is likely to be ineffective or unsafe in part or all of the paediatric population.

   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 annex 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

1. Waiver

1.1. Condition

Treatment of heart failure

The waiver applies to:

- the paediatric population from birth to less than 1 month of age;
- for film-coated tablet and for age-appropriate solid oral dosage form for oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

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 one month to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Film-coated tablet

Age-appropriate solid oral dosage form

2.1.4. Studies

Area	Number of studies	Description
Quality	1	**Study 1** Development of an age-appropriate solid oral dosage form.
Non-clinical	3	**Study 2** Mechanistic *in-vitro* study (1170517). **Study 3** 4-week dose range-finding juvenile rabbit bone toxicity study (1170514). **Study 4** 4-week investigative bone study in juvenile rats (1170516).

Clinical	4	**Study 5** Open-label, randomized, single-dose, multiple treatment period study to determine the relative bioavailability of LCZ696 paediatric formulation relative to the LCZ696 200 mg Final Market Image (FMI) tablet in healthy adult subjects (CLCZ696 B2126). **Study 6:** Open-label, single-dose, multi-centre study to evaluate the safety/tolerability and pharmacokinetics of LCZ696 in paediatric patients from one month to less than 18 years of age with heart failure (CLCZ696B2319 Part 1). **Study 7:** Double-blind, randomized, multi–centre, active controlled, parallel-group study to evaluate the safety and efficacy of LCZ696 vs. enalapril in paediatric patients from one month to less than 18 years of age with symptomatic left ventricular systolic dysfunction and heart failure (CLCZ696B2319 Part 2).

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 November 2021
Deferral for one or more studies contained in the paediatric investigation plan:	Yes