EMA/501292/2014

European Medicines Agency decision

P/0227/2014

of 5 September 2014

on the acceptance of a modification of an agreed paediatric investigation plan for aliskiren (Rasilez and associated names), (EMEA-000362-PIP01-08-M04) 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/253/2009 issued on 22 December 2009, and P/0237/2011 issued on 30 September 2011

Having regard to the application submitted by Novartis Europharm Limited on 22 May 2014 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 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 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 aliskiren (Rasilez and associated names), film-coated tablet, granules, 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 Novartis Europharm Limited, Wimblehurst Road, Horsham, West Sussex, RH12 5AB – Horsham, United Kingdom

Done at London, 5 September 2014

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

EMA/PDCO/368033/2014

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

EMEA-000362-PIP01-08-M04

Scope of the application

Active substance(s):

Aliskiren

Invented name:

Rasilez and associated names

Condition(s):

Treatment of hypertension

Treatment of heart failure

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Film-coated tablet

Granules

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Novartis Europharm Limited

Information about the authorised medicinal product:

See Annex II

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Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Novartis Europharm Limited submitted to the European Medicines Agency on 22 May 2014 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/253/2009 issued on 22 December 2009 and the decision P/0237/2011 issued on 30 September 2011.

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

The procedure started on 18 June 2014.

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.

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 (PIP)

1. Waiver

1.1. Condition:

Treatment of hypertension

The waiver applies to:

- children from birth to less than 2 year of age;
- for film-coated tablet for oral use and for granules for oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

1.2. Condition:

Treatment of heart failure

The waiver applies to:

- children from birth to less than 2 year of age;
- for film-coated tablet for oral use and for granules 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 hypertension

2.1.1. Indication(s) targeted by the PIP

Treatment of primary and secondary hypertension.

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

From 2 year to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Film-coated tablet

Granules

2.1.4. Studies

Area	Number of studies	Description
Quality-related studies	1	**Study 1:** Development of a film-coated mini-tablet (granules).

Non-clinical studies	2	**Study 2:** Juvenile development and toxicity study. **Study 3:** Juvenile development and toxicity study.
Clinical studies	4	**Study 4:** Relative bioavailability study of the paediatric and adult formulations. **Study 5:** Open-label, multiple-dose, multi-centre trial to evaluate pharmacokinetics, pharmacodynamics, safety and tolerability of aliskiren in children from 6 years to less than 18 years of age. **Study 6:** Multi-centre, randomized, double-blind trial to evaluate dose response, efficacy and safety of aliskiren in paediatric hypertensive patients from 6 years to less than 18 years of age with 52-week, randomised, double-dummy, dose-titrating extension of aliskiren and enalapril. **Study 7:** Multi-centre, double-blind, double-dummy, 12-week trial to evaluate pharmacokinetics, dose response, safety and tolerability of aliskiren compared with enalapril in children from 2 years to less than 8 years of age with secondary hypertension, with 48-week, open-label, dose-titrating extension of aliskiren and 4-week randomised, placebo-controlled withdrawal.

2.2. Condition:

Treatment of heart failure

2.2.1. Indication(s) targeted by the PIP

Treatment of heart failure.

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

From 2 year to less than 18 years of age.

2.2.3. Pharmaceutical form(s)

Film-coated tablet

Granules

2.2.4. Studies

Area	Number of studies	Description
Quality-related studies	1	**Study 1:** As for condition treatment of hypertension.
Non-clinical studies	2	**Study 2** and **study 3:** As for condition treatment of hypertension.

Clinical studies	4	**Study 4** and **study 5:** As for condition treatment of hypertension. **Study 8:** Survey of uses of medicinal products in children with heart failure. **Study 9:** Double-blind, randomized, parallel-group, multi-centre trial to evaluate safety and efficacy of aliskiren versus placebo in children from 2 years to less than 18 years of age.

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 December 2020
Deferral for one or more studies contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Treatment of hypertension

   Authorised indications:

- Treatment of essential hypertension in adults.

Authorised pharmaceutical form(s):

Film-coated tablet

Authorised route(s) of administration:

Oral use