European Medicines Agency

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EUROPEAN MEDICINES AGENCY DECISION

of 22 December 2009

on the agreement of a Paediatric Investigation Plan and on the granting of a deferral and on the granting of a waiver for aliskiren (Rasilez) (EMEA-000362-PIP01-08) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council as amended

(ONLY THE ENGLISH TEXT IS AUTHENTIC)

DISCLAIMER: This Decision does not entitle to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006, as amended.

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THE EUROPEAN MEDICINES AGENCY,

Having regard to the Treaty establishing the European Community,

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 as amended 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 Novartis Europharm Ltd. on 22 August 2008 under Article 16(1) of Regulation (EC) No 1901/2006 as amended 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 13 November 2009, in accordance with Article 18 of Regulation (EC) No 1901/2006 as amended, and Article 13 of said Regulation and of its own motion in accordance with Article 21 of said Regulation**,**

Having regard to Article 25 of Regulation (EC) No 1901/2006 as amended,

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 granting of a deferral and on the granting 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 granting a deferral.

(4) It is therefore appropriate to adopt a Decision granting 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 aliskiren (Rasilez), film-coated tablet and film-coated mini-tablet with appropriate dispensing device, 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 deferral for aliskiren (Rasilez), film-coated tablet and film-coated mini-tablet with appropriate dispensing device, 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 granted.

Article 3

A waiver for aliskiren (Rasilez), film-coated tablet and film-coated mini-tablet with appropriate dispensing device, 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 granted.

Article 4

This decision is addressed to Novartis Europharm Ltd., Wimblehurst Road, RH 12 5AB Horsham, United Kingdom.

Done at London, 22 December 2009

For the European Medicines Agency
Thomas Lönngren
Executive Director

(Signature on file)

European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

Doc. Ref. EMEA/PDCO/691183/2009
EMEA-000362-PIP01-08

OPINION OF THE PAEDIATRIC COMMITTEE ON THE AGREEMENT OF A PAEDIATRIC INVESTIGATION PLAN AND A DEFERRAL AND A WAIVER

Scope of the application

Active substance(s):
Aliskiren

(Invented) name:
Rasilez

Condition(s):
Hypertension
Heart failure

Pharmaceutical form(s):
Film-coated tablet
Film-coated mini-tablet with appropriate dispensing device

Route(s) of administration:
Oral use

Name/corporate name of the PIP applicant:
Novartis Europharm Ltd.

Information about the authorised medicinal product:
See Annex II

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Novartis Europharm Ltd. submitted for agreement to the EMEA on 22 August 2008 an application for a paediatric investigation plan for the above mentioned medicinal product and a waiver under Article 13 of said Regulation.

The procedure started on 25 September 2008.

Supplementary information was provided by the applicant on 4 September 2009.

A meeting with the Paediatric Committee took place on 11 November 2009.

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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 grant a deferral on its own motion in accordance with Article 21 of said Regulation,

- to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and 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 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 Agency, together with its annex(es) and appendix.

London, 13 November 2009

On behalf of the Paediatric Committee
Dr Daniel Brasseur, Chairman

(Signature on file)

ANNEX I

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

A. CONDITION(S)

Hypertension
Heart failure

B. WAIVER

- **Condition**

  Treatment of essential hypertension

  The waiver applies to:

  – children from birth to less than 6 months of age,
  – for film-coated tablet for oral use, and for mini-tablet for oral use,
  – on the grounds that the specific medicinal product is likely to be unsafe.

- **Condition**

  Heart failure

  The waiver applies to:

  – children from birth to less than 6 months of age,
  – for film-coated tablet for oral use, and for mini-tablet for oral use,
  – on the grounds that the specific medicinal product is likely to be unsafe.

C.1 PAEDIATRIC INVESTIGATION PLAN

- **Condition to be investigated**

  Hypertension

- **Proposed PIP indication**

  Treatment of primary and secondary hypertension

- **Subset(s) of the paediatric population concerned by the paediatric development**

  From 6 months to less than 18 years of age

- **Formulation(s)**

  Film-coated tablet for oral use
  Film-coated mini-tablet for oral use with appropriate dispensing device

- **Studies**

Area	Number of studies	Description
Quality	1	Film-coated mini-tablet
Non-clinical	2	Juvenile development and toxicity studies
Clinical	4	Relative bioavailability study of the paediatric and adult formulations

		Open-label, multiple-dose, multi-centre trial to evaluate pharmaco-kinetics, pharmacodynamics, safety and tolerability of aliskiren in children from 6 years to less than 18 years of age 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 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 1 year 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

C.2 PAEDIATRIC INVESTIGATION PLAN

- **Condition to be investigated**

  Heart failure

- **Proposed PIP indication**

  Treatment of heart failure

- **Subset(s) of the paediatric population concerned by the paediatric development**

  From 6 months to less than 18 years of age

- **Formulation(s)**

  Film-coated tablet for oral use
  Film-coated mini-tablet for oral use with appropriate dispensing device

- **Studies**

Area	Number of studies	Description
Quality	1	As for condition hypertension
Non-clinical	2	As for condition hypertension
Clinical	4	Relative bioavailability study of the paediatric and adult formulations Open-label, multiple-dose, multi-centre trial to evaluate pharmaco-kinetics, pharmacodynamics, safety and tolerability of aliskiren in children from 6 years to less than 18 years of age Survey of uses of medicinal products in children with heart failure Double-blind, randomized, parallel-group, multi-centre trial to evaluate safety and efficacy of aliskiren versus placebo in children from 6 months to less than 18 years of age.

Measures to address long term follow-up of potential safety issues in relation to paediatric use:	**Yes**
Date of completion of the paediatric investigation plan:	**By March 2017**
Deferral for some or all studies contained in the paediatric investigation plan:	**Yes**

ANNEX II

INFORMATION ABOUT THE AUTHORISED MEDICINAL PRODUCT

EU Number	Invented name	Strength	Pharmaceutical Form	Route of Administration	Packaging	Content (concentration)	Package size
EU/1/07/405/001	Rasilez	150 mg	Film-coated tablet	Oral use	blister (PA/alu/PVC)		7 tablets
EU/1/07/405/002	Rasilez	150 mg	Film-coated tablet	Oral use	blister (PA/alu/PVC)		14 tablets
EU/1/07/405/003	Rasilez	150 mg	Film-coated tablet	Oral use	blister (PA/alu/PVC)		28 tablets
EU/1/07/405/004	Rasilez	150 mg	Film-coated tablet	Oral use	blister (PA/alu/PVC)		30 tablets
EU/1/07/405/005	Rasilez	150 mg	Film-coated tablet	Oral use	blister (PA/alu/PVC)		50 tablets
EU/1/07/405/006	Rasilez	150 mg	Film-coated tablet	Oral use	blister (PA/alu/PVC)		56 tablets
EU/1/07/405/007	Rasilez	150 mg	Film-coated tablet	Oral use	blister (PA/alu/PVC)		84 (3 x 28) tablets
EU/1/07/405/008	Rasilez	150 mg	Film-coated tablet	Oral use	blister (PA/alu/PVC)		90 tablets
EU/1/07/405/009	Rasilez	150 mg	Film-coated tablet	Oral use	blister (PA/alu/PVC)		98 (2 x 49) tablets
EU/1/07/405/010	Rasilez	150 mg	Film-coated tablet	Oral use	blister (PA/alu/PVC)		280 (20 x 14) tablets
EU/1/07/405/011	Rasilez	300 mg	Film-coated tablet	Oral use	blister (PA/alu/PVC)		7 tablets
EU/1/07/405/012	Rasilez	300 mg	Film-coated tablet	Oral use	blister (PA/alu/PVC)		14 tablets
EU/1/07/405/013	Rasilez	300 mg	Film-coated tablet	Oral use	blister (PA/alu/PVC)		28 tablets
EU/1/07/405/014	Rasilez	300 mg	Film-coated tablet	Oral use	blister (PA/alu/PVC)		30 tablets
EU/1/07/405/015	Rasilez	300 mg	Film-coated tablet	Oral use	blister (PA/alu/PVC)		50 tablets
EU/1/07/405/016	Rasilez	300 mg	Film-coated tablet	Oral use	blister (PA/alu/PVC)		56 tablets
EU/1/07/405/017	Rasilez	300 mg	Film-coated tablet	Oral use	blister (PA/alu/PVC)		84 (3 x 28) tablets
EU/1/07/405/018	Rasilez	300 mg	Film-coated tablet	Oral use	blister (PA/alu/PVC)		90 (3 x 30) tablets
EU/1/07/405/019	Rasilez	300 mg	Film-coated tablet	Oral use	blister (PA/alu/PVC)		98 (2 x 49) tablets
EU/1/07/405/020	Rasilez	300 mg	Film-coated tablet	Oral use	blister (PA/alu/PVC)		280 (20 x 14) tablets