EMA/708577/2011

European Medicines Agency decision

P/237/2011

of 30 September 2011

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

Having regard to the application submitted by Novartis Europharm Limited on 27 May 2011 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 12 August 2011, 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 and to the waiver.

(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 and the 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 aliskiren (Rasilez and associated names), film-coated tablet, granules, oral use, including changes to the deferral, and the waiver, 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 Limted, Wimblehurst Road, Horsham, West Sussex, RH12 5AB Horsham, United Kingdom.

Done at London, 30 September 2011

For the European Medicines Agency
Andreas Pott
Acting Executive Director
(Signature on file)

EMA/PDCO/586120/2011

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

EMEA-000362-PIP01-08-M01

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 27 May 2011 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.

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

The procedure started on 15 June 2011.

A meeting with the Paediatric Committee took place on 11 August 2011.

Scope of the modification

The scope of the waiver, details of some paediatric trials and timelines of some measures were 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 and to the waiver in the scope set out in the Annex I of this opinion.

   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 paediatric investigation plan and the subsets of the paediatric population and conditions 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, 12 August 2011

On behalf of the Paediatric Committee
Dr Daniel Brasseur, 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

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 for oral use.

Granules

2.1.4. Studies

Area	Number of studies	Description
Quality	1	Study 1: Development of a film-coated mini-tablet (granules).
Non-clinical	2	Study 2: Juvenile development and toxicity study. Study 3: Juvenile development and toxicity study.
Clinical	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 for oral use.

Film-coated mini-tablet (granules) for oral use with pre-filled dispensing capsules

2.2.4. Studies

Area	Number of studies	Description
Quality	1	Study 1: As for condition treatment of hypertension.
Non-clinical	2	Study 2 and study 3: As for condition treatment of hypertension.
Clinical	4	Study 4: As for condition treatment of hypertension. 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 March 2017
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.

EU Number	(Invented) name	Strength	Pharmaceutical Form	Route of Administration	Packaging	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

EU/1/07/405/021	Rasilez	150 mg	Film-coated tablet	Oral use	blister (PCTFE/PVC)	14 tablets
EU/1/07/405/022	Rasilez	150 mg	Film-coated tablet	Oral use	blister (PCTFE/PVC)	28 tablets
EU/1/07/405/023	Rasilez	150 mg	Film-coated tablet	Oral use	blister (PCTFE/PVC)	30 tablets
EU/1/07/405/024	Rasilez	150 mg	Film-coated tablet	Oral use	blister (PCTFE/PVC)	50 tablets
EU/1/07/405/025	Rasilez	150 mg	Film-coated tablet	Oral use	blister (PCTFE/PVC)	56 tablets
EU/1/07/405/026	Rasilez	150 mg	Film-coated tablet	Oral use	blister (PCTFE/PVC perforated unit-dose)	56 x 1 tablets
EU/1/07/405/027	Rasilez	150 mg	Film-coated tablet	Oral use	blister (PCTFE/PVC)	90 tablets
EU/1/07/405/028	Rasilez	150 mg	Film-coated tablet	Oral use	blister (PCTFE/PVC)	98 tablets
EU/1/07/405/029	Rasilez	150 mg	Film-coated tablet	Oral use	blister (PCTFE/PVC perforated unit-dose)	98 (2 x 49 x 1) tablets
EU/1/07/405/030	Rasilez	150 mg	Film-coated tablet	Oral use	blister (PCTFE/PVC)	280 (20 x 14) tablets
EU/1/07/405/031	Rasilez	300 mg	Film-coated tablet	Oral use	blister (PCTFE/PVC)	14 tablets
EU/1/07/405/032	Rasilez	300 mg	Film-coated tablet	Oral use	blister (PCTFE/PVC)	28tablets
EU/1/07/405/033	Rasilez	300 mg	Film-coated tablet	Oral use	blister (PCTFE/PVC)	30 tablets
EU/1/07/405/034	Rasilez	300 mg	Film-coated tablet	Oral use	blister (PCTFE/PVC)	50 tablets
EU/1/07/405/035	Rasilez	300 mg	Film-coated tablet	Oral use	blister (PCTFE/PVC)	56 tablets
EU/1/07/405/036	Rasilez	300 mg	Film-coated tablet	Oral use	blister (PCTFE/PVC perforated unit-dose)	56 x 1 tablets
EU/1/07/405/037	Rasilez	300 mg	Film-coated tablet	Oral use	blister (PCTFE/PVC)	90 tablets
EU/1/07/405/038	Rasilez	300 mg	Film-coated tablet	Oral use	blister (PCTFE/PVC)	98 tablets
EU/1/07/405/039	Rasilez	300 mg	Film-coated tablet	Oral use	blister (PCTFE/PVC perforated unit-dose)	98 (2 x 49 x 1) tablets
EU/1/07/405/040	Rasilez	300 mg	Film-coated tablet	Oral use	blister (PCTFE/PVC)	280 (20 x 14) tablets