EMA/339546/2012

European Medicines Agency decision

P/0087/2012

of 25 May 2012

on the acceptance of a modification of an agreed paediatric investigation plan for macitentan (EMEA-001032-PIP01-10-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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on the acceptance of a modification of an agreed paediatric investigation plan for macitentan (EMEA-001032-PIP01-10-M01) 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/303/2011 issued on 21 December 2011,

Having regard to the application submitted by Actelion Registration Ltd on 20 February 2012 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 13 April 2012, 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 macitentan, dispersible tablet, film-coated tablet, 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 Actelion Registration Ltd, 389 Chiswick High Road, W44 4AL - London, United Kingdom.

Done at London, 25 May 2012

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

EMA/PDCO/162937/2012

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

EMEA-001032-PIP01-10-M01

Scope of the application

Active substance(s):

Macitentan

Invented name:

Condition(s):

Treatment of pulmonary arterial hypertension

Treatment of systemic sclerosis

Treatment of idiopathic pulmonary fibrosis

Pharmaceutical form(s):

Dispersible tablet

Film-coated tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Actelion Registration Ltd

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Actelion Registration Ltd submitted to the European Medicines Agency on 20 February 2012 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/303/2011 issued on 21 December 2011.

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

The procedure started on 19 March 2012.

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Scope of the modification

Some 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 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 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(es) and appendix.

London, 13 April 2012

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 systemic sclerosis

The waiver applies to:

- All subsets of the paediatric population from birth to less than 18 years of age;
- for dispersible tablet and film-coated tablet, oral use;
- on the grounds that the disease or condition for which the specific medicinal product is intended occurs only in adult populations.

1.2. Condition: Treatment of idiopathic pulmonary fibrosis

The waiver applies to:

- All subsets of the paediatric population from birth to less than 18 years of age;
- for dispersible tablet and film-coated tablet, oral use;
- on the grounds that the disease or condition for which the specific medicinal product is intended occurs only in adult populations.

2. Paediatric Investigation Plan

2.1. Condition: Treatment of pulmonary arterial hypertension

2.1.1. Indication(s) targeted by the PIP

Treatment of pulmonary arterial hypertension (PAH)

Treatment of persistent pulmonary hypertension of the newborn (PPHN)

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)

Dispersible tablet

Film-coated tablet

2.1.4. Studies

Area	Number of studies	Description
Quality	2	Study 1: Development of a dispersible tablet formulation. Study 2: Study of nasogastric tube administration of the dispersible tablet formulation in vitro.
Non-clinical	2	Study 3: 25 day dose range finding toxicity study in juvenile rats. Study 4: 67 day toxicity study in juvenile rats.
Clinical	3	Study 5: Double-blind, randomised, multicentre, placebo-controlled (add-on to standard of care) trial to evaluate efficacy, safety, tolerability and pharmacokinetics of macitentan in children from 7 to less than 18 years of age with pulmonary arterial hypertension. Study 6: Double-blind, randomised, multicentre, placebo-controlled (add-on to standard of care) trial to evaluate efficacy, safety, tolerability and pharmacokinetics of macitentan in children from 1 month to less than 7 years of age with pulmonary arterial hypertension.

Area	Number of studies	Description
		Study 7: Double blind, randomised, multicentre, placebo controlled (add-on to inhaled nitric oxide) trial to evaluate efficacy, safety, tolerability and pharmacokinetics of macitentan in neonates with persistent pulmonary hypertension of the newborn (PPHN).

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety issues in relation to paediatric use:	No.
Date of completion of the paediatric investigation plan:	By September 2018.
Deferral for one or more studies contained in the paediatric investigation plan:	Yes.