EMA/982770/2011

European Medicines Agency decision

P/303/2011

of 21 December 2011

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for macitentan (EMEA-001032-PIP01-10) 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 application submitted by Actelion Registration Ltd on 5 August 2010 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 11 November 2011, in accordance with Article 18 of Regulation (EC) No 1901/2006, and Article 21 of said Regulation 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 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 macitentan, dispersible tablet, film-coated tablet, 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 macitentan, dispersible tablet, film-coated tablet, 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 macitentan, dispersible tablet, film-coated tablet, 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 Actelion Registration Ltd, 389 Chiswick High Road, W44 4AL - London, United Kingdom.

Done at London, 21 December 2011

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

EMA/763214/2011

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and a waiver

EMEA-001032-PIP01-10

Scope of the application

Active substance(s):

Macitentan

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 16(1) of Regulation (EC) No 1901/2006 as amended, Actelion Registration Ltd submitted for agreement to the European Medicines Agency on 5 August 2010 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 15 September 2010.

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Supplementary information was provided by the applicant on 25 August 2011.

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 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)(b) of said Regulation, on the grounds that the disease or condition for which the specific medicinal product is intended occurs only in adult populations.

     The Icelandic and the Norwegian Paediatric Committee member(s) agree(s) 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 European Medicines Agency, together with its annex(es) and appendix.

London, 11 November 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 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.