EMA/255881/2012

European Medicines Agency decision

P/0074/2012

of 25 April 2012

on the acceptance of a modification of an agreed paediatric investigation plan for treprostinil (remodulin and associated names), (EMEA-000207-PIP01-08-M02) 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/121/2008 issued on 1 December 2008,

Having regard to the application submitted by United Therapeutics Europe Ltd on 16 December 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 9 March 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 treprostinil (remodulin and associated names), nebuliser solution, solution for infusion, inhalation use, subcutaneous use, intravenous 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 United Therapeutics Europe Ltd, Unither House, Curfew Bell Road, KT16 9FG, Chertsey, United Kingdom.

Done at London, 25 April 2012

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

EMA/PDCO/25181/2012

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

EMEA-000207-PIP01-08-M02

Scope of the application

Active substance(s):

Treprostinil

Invented name:

Remodulin and associated names

Condition(s):

Treatment of Pulmonary Arterial Hypertension

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Nebuliser solution

Solution for infusion

Route(s) of administration:

Inhalation use

Subcutaneous use

Intravenous use

Name/corporate name of the PIP applicant:

United Therapeutics Europe Ltd

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, United Therapeutics Europe Ltd submitted to the European Medicines Agency on 16 December 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/121/2008 issued on 1 December 2008.

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

The procedure started on 12 January 2012.

Scope of the modification

Some measures 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 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 annex(es) and appendix.

London, 9 March 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 Pulmonary Arterial Hypertension

The waiver applies to:

- Infants and children from birth to less than 2 years;
- for nebuliser solution for inhalation administration;
- on the grounds that the specific medicinal product is likely to be ineffective.

And to:

- Children from birth to less than 12 years;
- for solution for infusion, subcutaneous route;
- on the grounds that clinical studies cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the paediatric population.

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.

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)

Nebuliser solution for inhalation.

Solution for infusion, subcutaneous route.

Solution for infusion, intravenous route.

2.1.4. Studies

Area	Number of studies	Description
Quality	2	Study 1: Development of an age-appropriate inhalation device for children from 2 years old to less than 6 years old. Study 2: Development of an intravenous formulation.
Non-clinical	0	Not applicable.
Clinical	5	Study 3: Randomized, double blind, placebo controlled add-on to baseline

Area	Number of studies	Description
		therapy, multiple-dose, parallel group study of the safety and efficacy of inhaled treprostinil sodium using an Inhalation Device in paediatric patients from 6 years to less than 18 years old with pulmonary arterial hypertension. Study 4: Open-label safety and tolerability study using an age-appropriate inhalation device, in paediatric patients from 2 years to less than 6 years old with pulmonary arterial hypertension. Study 5: Randomized, double-blind, placebo controlled add-on to baseline therapy study using an age-appropriate inhalation device, in paediatric patients from 2 years to less than 6 years old with pulmonary arterial hypertension. Study 6: Analyses of existing data to clarify the safety and efficacy of the parenteral formulation of treprostinil in children aged from 12 to less than 18 years, as systematic review. Study 7: A comparative study of intravenously administered treprostinil in neonates or older children with acute Pulmonary Arterial Hypertension treated in Paediatric Intensive Care Unit.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	No.
Date of completion of the paediatric investigation plan:	By December 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 Pulmonary Arterial Hypertension

   Authorised indications:

   Treatment of idiopathic or heritable pulmonary arterial hypertension (PAH) to improve exercise tolerance and symptoms of the disease in patients classified as NYHA (New York Heart Association) Class III

Invented name	Strength	Pharmaceutical Form	Route of administration
Remodulin and associated names	1 mg/ml 2.5 mg/ml 5 mg/ml 10 mg/ml	Solution for Infusion	Subcutaneous use