



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/111310/2015

European Medicines Agency decision

P/0059/2015

of 1 April 2015

on the refusal of a modification of an agreed paediatric investigation plan for treprostinil (Remodulin and associated names) (EMEA-000207-PIP01-08-M05) 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 726/2004¹,

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 Agency²,

Having regard to the European Medicines Agency's decision P/121/2008 issued on 1 December 2008, the decision P/0074/2012 issued on 25 April 2012, the decision P/0291/2012 issued on 18 December 2012, and the decision P/0308/2013 issued on 19 December 2013,

Having regard to the application submitted by United Therapeutics Europe Limited on 24 November 2014 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 February 2015, 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 refusal of changes to the agreed paediatric investigation plan.
- (2) It is therefore appropriate to adopt a decision on the refusal 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), solution for infusion, subcutaneous use, intravenous 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, are hereby refused.

Article 2

This decision is addressed to United Therapeutics Europe Limited, Unither House, Curfew Bell Road, KT16 9FG – Chertsey, United Kingdom.

Done at London, 1 April 2015

For the European Medicines Agency
Jordi Llinares Garcia
Head of Division (ad interim)
Human Medicines Research and Development Support
(Signature on file)



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/PDCO/753954/2014

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

EMA-000207-PIP01-08-M05

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):

Solution for infusion

Route(s) of administration:

Subcutaneous use

Intravenous use

Name / corporate name of the PIP applicant:

United Therapeutics Europe Limited

Information about the authorised medicinal product:

See Annex II



Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, United Therapeutics Europe Limited submitted to the European Medicines Agency on 24 November 2014 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 decision P/0074/2012 issued on 25 April 2012, the decision P/0291/2012 issued on 18 December 2012, and the decision P/0308/2013 issued on 19 December 2013.

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

The procedure started on 16 December 2014.

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 refuse the changes proposed by the applicant regarding the paediatric investigation plan.

The Norwegian Paediatric Committee member agrees 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 remain unchanged and are set out in the Annex I.
3. The scientific conclusions and the grounds for refusal are set out in the summary report appended to this opinion.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annexes and appendix.

London, 13 February 2015

On behalf of the Paediatric Committee
Dr Dirk Mentzer, 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 (PIP)

1. Waiver

1.1. Condition:

Treatment of pulmonary arterial hypertension

The waiver applies to:

- children from one month 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 one month of age and from 12 to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Solution for infusion

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	Study 1: Development of an intravenous formulation.
Non-clinical studies	0	Not applicable.
Clinical studies	1	Study 3: A comparative study of intravenously administered treprostinil in neonates with Persistent Pulmonary Hypertension of neonates (PPHN) treated in Paediatric Intensive Care Unit.

Extrapolation, modelling and simulation studies	0	Not applicable.
Other studies	1	Study 2: 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.
Other measures	0	Not applicable.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	No.
Date of completion of the paediatric investigation plan:	By December 2017.
Deferral for one or more measures 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.

Authorised pharmaceutical form(s):

Solution for infusion

Authorised route(s) of administration:

Subcutaneous use, intravenous use