EMA/478172/2012

European Medicines Agency decision
P/0158/2012

of 25 July 2012

on the acceptance of a modification of an agreed paediatric investigation plan for sildenafil (Revatio), (EMEA-000671-PIP01-09-M03) 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.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7040
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

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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/33/2010 issued on 17 March 2010, the decision P/114/2011 issued on 6 May 2011, and the decision P/0070/2012 issued on 4 April 2012,

Having regard to the application submitted by Pfizer Limited on 26 March 2012 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 8 June 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 sildenafil (Revatio), film-coated tablet, powder for oral suspension, solution for injection, oral 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 Pfizer Limited, Ramsgate Road, Sandwich, Kent, CT13 9NJ Sandwich, United Kingdom.

Done at London, 25 July 2012

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

EMA/PDCO/348687/2012

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

EMEA-000671-PIP01-09-M03

Scope of the application

Active substance(s):

Sildenafil

Invented name:

Revatio

Condition(s):

Treatment of pulmonary arterial hypertension

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Film-coated tablet

Powder for oral suspension

Solution for injection

Route(s) of administration:

Oral use

Intravenous use

Name/corporate name of the PIP applicant:

Pfizer 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, Pfizer Limited submitted to the European Medicines Agency on 26 March 2012 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/33/2010 issued on 17 March 2010, the decision P/114/2011 issued on 6 May 2011, and the decision P/0070/2012 issued on 4 April 2012.

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

The procedure started on 16 April 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 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 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, 8 June 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

Not applicable.

2. Paediatric Investigation Plan

2.1. Condition: Treatment of pulmonary arterial hypertension

2.1.1. Indication(s) targeted by the PIP

Treatment of Persistent Pulmonary Hypertension of the Newborn (PPHN)

Treatment of Pulmonary Arterial Hypertension (PAH)

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From birth to less than 18 years

- Birth to less than 1 month of age: PPHN.
- From 1 month to less than 18 years of age: PAH.

2.1.3. Pharmaceutical form(s)

Film-coated tablet for oral use in children 6 years and older

Powder for oral suspension for children less than 6 years of age

Solution for injection 0.8 mg/mL in 20 mL and 50 mL vials

2.1.4. Studies

Area	Description
Quality	1. Powder for oral suspension for children less than 6 years of age.
Non-clinical	Not applicable.
Clinical	**Pulmonary Arterial Hypertension** 2. A1481131: Randomized, double-blind, placebo-controlled, dose-ranging, parallel group study of oral sildenafil in the treatment of children with pulmonary arterial hypertension. 3. A1481156: A multicentre long-term extension study to assess the safety of oral sildenafil in the treatment of subjects who have completed study A1481131. **Persistent Pulmonary Hypertension of the Newborn.** 4. A1481157: 7-day open-label, multicentre pharmacokinetic study of sildenafil in newborns with persistent pulmonary hypertension. 5. A1481316: Multicentre, randomized, blinded, controlled, 2-arm, parallel-group study to evaluate the efficacy and safety of the combination of IV sildenafil and iNO for the treatment of neonates with PPHN or hypoxic respiratory failure at

Area	Description
	risk for PPHN

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes.
Date of completion of the paediatric investigation plan:	By July 2014.
Deferral for some or all 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 patients with pulmonary arterial hypertension classified as WHO functional class II and III to improve exercise capacity.

EU Number	(Invented) name	Strength	Pharmaceutical Form	Route of Administration	Packaging	Content (concentration)	Package size
EU/1/05/318/001	Revatio	20 mg	Film-coated tablet	Oral use	blister (PVC/alu)		90 tablets
EU/1/05/318/002	Revatio	0.8 mg/ml	Solution for injection	Intravenous use	vial (glass)	20 ml	1 vial