European Medicines Agency

Doc. Ref. EMA/159661/2010
P/33/2010

**EUROPEAN MEDICINES AGENCY DECISION**

**of 17 March 2010**

**on the agreement of a Paediatric Investigation Plan and on the granting of a deferral and on the refusal of a waiver for Sildenafil citrate (Revatio) (EMEA-000671-PIP01-09) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council as amended**

(ONLY THE ENGLISH TEXT IS AUTHENTIC)

*DISCLAIMER: This Decision does not entitle to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006, as amended.*

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THE EUROPEAN MEDICINES AGENCY,

Having regard to the Treaty establishing the European Community,

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 as amended 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 Pfizer Limited on 24 July 2009 under Article 16(1) of Regulation (EC) No 1901/2006 as amended also requesting a waiver under Article 13 of said Regulation and a deferral under Article 20 of said Regulation,

Having regard to the Opinion of the Paediatric Committee of the European Medicines Agency, issued on 16 October 2009, in accordance with Article 18 of Regulation (EC) No 1901/2006 as amended, and Article 21 of said Regulation**,**

Having regard to Article 25 of Regulation (EC) No 1901/2006 as amended,

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 refusal 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 refusing 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 Sildenafil citrate (Revatio), film-coated tablet, powder for oral suspension and solution for injection, oral use and 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, is hereby agreed.

*Article 2*

A deferral for Sildenafil citrate (Revatio), film-coated tablet, powder for oral suspension and solution for injection, oral use and 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, is hereby granted.

*Article 3*

A waiver for Sildenafil citrate (Revatio), film-coated tablet, powder for oral suspension and solution for injection, oral use and 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, is hereby refused.

*Article 4*

This decision is addressed to Pfizer Limited, Ramsgate Road, Sandwich, CT13 9NJ United Kingdom.

Done at London, 17 March 2010

For the European Medicines Agency
Thomas Lönngren
Executive Director

(Signature on file)

European Medicines Agency
*Pre-authorisation Evaluation of Medicines for Human Use*

Doc. Ref. EMEA/PDCO/652199/2009
EMEA-000671-PIP01-09

# OPINION OF THE PAEDIATRIC COMMITTEE ON THE AGREEMENT OF A PAEDIATRIC INVESTIGATION PLAN AND A DEFERRAL AND ON THE REFUSAL OF A WAIVER

## Scope of the application

Active substance(s):
Sildenafil citrate

(Invented) name:
Revatio

Condition(s):
Pulmonary Arterial Hypertension

Pharmaceutical forms:
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

## Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Pfizer Limited submitted for agreement to the EMEA on 24 July 2009 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 20 August 2009.

A meeting with the Paediatric Committee took place on 14 October 2009.

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**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 refuse the granting of a waiver in accordance with Article 13 of said Regulation, for some of the subsets of the paediatric population as it does not meet the grounds detailed in Article 11(1) of said Regulation.

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 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 Agency, together with its annex(es) and appendix.

London, 16 October 2009

On behalf of the Paediatric Committee
Dr Daniel Brasseur, Chairman

(Signature on file)

## ANNEX I

## 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

## A. CONDITION(S)

Pulmonary Arterial Hypertension

## B. WAIVER

Not applicable.

## C. PAEDIATRIC INVESTIGATION PLAN

- **Condition to be investigated**

Pulmonary Arterial Hypertension

- **Proposed PIP indication**

Persistent Pulmonary Hypertension of the Newborn (PPHN)
Pulmonary Arterial Hypertension (PAH)

- **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

- **Formulation(s)**

Film-coated tablet 20 mg for oral use in children 6 years and older
Powder for oral suspension 10 mg/mL suspension for children less than 6 years of age
Solution for injection 0.8 mg/mL in 20 mL and 50 mL vials

- **Studies**

| Area | Number of studies | Description |
|---|---|---|
| Quality | | Powder for oral suspension for children less than 6 years of age |
| Non-clinical | | Not applicable. |
| Clinical | 4 | **Pulmonary Arterial Hypertension**<br>A1481131: Randomized, double-blind, placebo-controlled, dose-ranging, parallel group study of oral sildenafil in the treatment of children with pulmonary arterial hypertension<br><br>A1481156: A multicentre long-term extension study to assess the safety of oral sildenafil in the treatment of subjects who have completed study A1481131<br><br>**Persistent Pulmonary Hypertension of the Newborn**<br>A1481157: 7-day open-label, multicentre pharmacokinetic study of sildenafil in newborns with persistent pulmonary hypertension<br><br>A1481276: Individually matched control, open-label, single arm single center study with associated long term follow-up to investigate safety and efficacy of sildenafil in near term and term newborns with persistent pulmonary hypertension of the newborn (PPHN) |

| | |
|---|---|
| **Measures to address long term follow-up of potential safety issues and efficacy in relation to paediatric use:** | **Yes** |
| **Date of completion of the paediatric investigation plan:** | **By 3Q2013** |
| **Deferral for some or all studies contained in the paediatric investigation plan:** | **Yes** |

**ANNEX II**

**INFORMATION ABOUT THE AUTHORISED MEDICINAL PRODUCT**

| **EU Number** | **Invented name** | **Strength** | **Pharmaceutical Form** | **Route of Administration** | **Packaging** | **Package size** |
|---|---|---|---|---|---|---|
| EU/1/05/318/001 | Revatio | 20 mg | Film-coated tablet | Oral use | blister (PVC/alu) | 90 tablets |