EMA/831890/2018

European Medicines Agency decision

P/0016/2019

of 3 January 2019

on the acceptance of a modification of an agreed paediatric investigation plan for sildenafil (Revatio), (EMEA-000671-PIP01-09-M10) 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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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, the decision P/0070/2012 issued on 4 April 2012, the decision P/0158/2012 issued on 25 July 2012, the decision P/0165/2013 issued on 29 July 2013, the decision P/0196/2014 issued on 8 August 2014, decision P/0092/2015 issued on 8 May 2015 and the decision P/0382/2017 issued on 19 December 2017,

Having regard to the application submitted by Pfizer Limited on 10 August 2018 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 16 November 2018, 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 and to the deferral.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, including changes to the deferral.

[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, including changes to the deferral, 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, CT13 9NJ - Sandwich, United Kingdom.

EMA/PDCO/570653/2018
London, 16 November 2018

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

EMEA-000671-PIP01-09-M10

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 10 August 2018 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, the decision P/0070/2012 issued on 4 April 2012, the decision P/0158/2012 issued on 25 July 2012, the decision P/0165/2013 issued on 29 July 2013, the decision P/0196/2014 issued on 8 August 2014, decision P/0092/2015 issued on 8 May 2015 and the decision P/0382/2017 issued on 19 December 2017.

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

The procedure started on 18 September 2018.

Scope of the modification

Some measures and timelines 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 and to the deferral 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 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 annexes and appendix.

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

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

Powder for oral suspension

Solution for injection

2.1.4. Studies

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Powder for oral suspension for children less than 6 years of age.
Non-clinical studies	0	Not applicable.
Clinical studies	4	**Pulmonary arterial hypertension** **Study 2** A1481131: Randomized, double-blind, placebo-controlled, dose-ranging, parallel group study of oral sildenafil in the treatment of children with pulmonary arterial hypertension. **Study 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 **Study 4** A1481157: 7-day open-label, multicentre pharmacokinetic study of sildenafil in newborns with persistent pulmonary hypertension. **Study 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 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 February 2019
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 indication(s):

- Adults

  Treatment of adult patients with pulmonary arterial hypertension classified as WHO functional class II and III, to improve exercise capacity. Efficacy has been shown in primary pulmonary hypertension and pulmonary hypertension associated with connective tissue disease.

- Paediatric population

  Treatment of paediatric patients aged 1 year to 17 years old with pulmonary arterial hypertension. Efficacy in terms of improvement of exercise capacity or pulmonary haemodynamics has been shown in primary pulmonary hypertension and pulmonary hypertension associated with congenital heart disease.

Authorised pharmaceutical form(s)

Film-coated tablets

Powder for oral suspension

Solution for injection

Authorised route(s) of administration

Oral use

Intravenous use