EMA/265075/2016

European Medicines Agency decision

P/0127/2016

of 20 May 2016

on the acceptance of a modification of an agreed paediatric investigation plan for tadalafil (Adcirca, Cialis), (EMEA-000452-PIP02-10-M04) 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/108/2011 issued on 6 May 2011, the decision P/0118/2012 issued on 2 July 2012, the decision P/0229/2014 issued on 5 September 2014, and the decision P/0165/2015 issued on 7 August 2015,

Having regard to the application submitted by Eli Lilly and Company Ltd on 22 December 2015 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 1 April 2016, 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 tadalafil (Adcirca, Cialis), film-coated tablet, oral suspension, oral use, gastric 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 Eli Lilly and Company Ltd, Erl Wood Manor, Sunninghill Road, GU20 6PH - Windlesham, Surrey, United Kingdom.

Done at London, 20 May 2016

For the European Medicines Agency
Zaïde Frias
Head of Division
Human Medicines Research and Development Support
(Signature on file)

EMA/PDCO/19935/2016
London, 1 April 2016

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

EMEA-000452-PIP02-10-M04

Scope of the application

Active substance(s):

Tadalafil

Invented name:

Adcirca

Cialis

Condition(s):

Treatment of pulmonary arterial hypertension

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Film-coated tablet

Oral suspension

Route(s) of administration:

Oral use

Gastric use

Name/corporate name of the PIP applicant:

Eli Lilly and Company 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, Eli Lilly and Company Ltd submitted to the European Medicines Agency on 22 December 2015 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/108/2011 issued on 6 May 2011, the decision P/0118/2012 issued on 2 July 2012, the decision P/0229/2014 issued on 5 September 2014, and the decision P/0165/2015 issued on 7 August 2015.

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

The procedure started on 2 February 2016.

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 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 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

1.1. Condition:

Treatment of pulmonary arterial hypertension

The waiver applies to:

- all subsets of the paediatric population from 1 month to less than 6 months of age;
- film-coated tablet, oral suspension, oral use, gastric use;
- 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 (PAH)

Treatment of persistent pulmonary hypertension of the newborn (PPHN)

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

- From birth to less than 1 month of age
- From 6 months to less than 18 years

2.1.3. Pharmaceutical form(s)

Film-coated tablets, oral suspension

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Study on nasogastric tube administration of the tadalafil suspension to provide data on the accuracy of the dosage
Non-clinical studies	0	Not applicable.

Area	Number of measures	Description
Clinical studies	5	**Study 2** Open-label, randomised, single-dose trial in healthy adult subjects to evaluate bioavailability of a tadalafil suspension (2 mg/ml) compared to marketed tadalafil film-coated tablets. **Study 3** Open-label multicentre, 2-period, multiple ascending dose trial to evaluate pharmacokinetics and safety of tadalafil administered orally in children from 6 months to less than 18 years with pulmonary arterial hypertension (PAH) with an open-label long-term extension. **Study 4** Randomised multicentre, double-blind, add on, 2-period study to evaluate efficacy and long-term safety of tadalafil administered once daily as a tablet or suspension to children from 6 months to less than 18 years of age with PAH with an open-label long-term extension. **Study 5** Open-label, multicentre, single dose, study of 3 dose cohorts to evaluate safety and pharmacokinetics of tadalafil administered by nasogastric tube as suspension to neonates with persistent pulmonary hypertension (PPHN) during weaning from inhaled nitric oxide (iNO). **Study 6** Randomised, double-blind, multicentre, add-on, placebo controlled -study to evaluate the efficacy and safety of tadalafil administered by nasogastric tube as a suspension in neonates with persistent pulmonary hypertension (PPHN) during weaning from inhaled nitric oxide (iNO)
Extrapolation, modelling and simulation studies	0	Not applicable.
Other studies	0	Not applicable.
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:	Yes
Date of completion of the paediatric investigation plan:	By March 2021
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 pulmonary arterial hypertension (PAH) in adults classified as WHO functional class II and III, to improve exercise capacity. Efficacy has been shown in idiopathic PAH (IPAH) and in PAH related to collagen vascular disease.

Authorised pharmaceutical form(s):

Film-coated tablet

Authorised route(s) of administration:

Oral use