EMA/343619/2011

European Medicines Agency decision

P/108/2011

of 6 May 2011

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for tadalafil (Adcirca, Cialis), (EMEA-000452-PIP02-10) 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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on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for tadalafil (Adcirca, Cialis), (EMEA-000452-PIP02-10) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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 application submitted by Eli Lilly and Company Limited on 9 April 2010 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 18 March 2011, in accordance with Article 18 of Regulation (EC) No 1901/2006, and Article 21 of said Regulation and Article 13 of said Regulation,

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 agreement of a paediatric investigation plan and on the granting of a deferral and on the granting 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 granting 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 tadalafil (Adcirca, Cialis), film-coated tablet, oral suspension, oral use, gastric 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 tadalafil (Adcirca, Cialis), film-coated tablet, oral suspension, oral use, gastric 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 tadalafil (Adcirca, Cialis), film-coated tablet, oral suspension, oral use, gastric 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 4

This decision is addressed to Eli Lilly and Company Limited, Erl Wood Manor, Sunninghill Road, GU20 6PH - Windlesham, Surrey, United Kingdom.

Done at London, 6 May 2011

For the European Medicines Agency
Andreas Pott
Acting Executive Director
(Signature on file)

EMA/PDCO/82100/2011

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and a waiver

EMEA-000452-PIP02-10

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 Limited

Information about the authorised medicinal product:

See Annex II

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Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Eli Lilly and Company Limited submitted for agreement to the European Medicines Agency on 9 April 2010 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 May 2010.

Supplementary information was provided by the applicant on 7 January 2011. The applicant proposed modifications to the paediatric investigation plan.

A meeting with the Paediatric Committee took place on 17 March 2011.

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 grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

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

London, 18 March 2011

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

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;
- for 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

2.2. Indication(s) targeted by the PIP

Treatment of pulmonary arterial hypertension (PAH)

Treatment of Persistent pulmonary hypertension of the newborn (PPHN)

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

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

2.4. Pharmaceutical form(s)

Film-coated tablets, oral suspension.

2.5. Studies

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

Area	Number of studies	Description
		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, dose-escalation study 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).

3. Follow-up, completion and deferral of PIP

Measures to address long term follow-up of potential safety issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By March 2020
Deferral for one or more studies contained in the paediatric investigation plan:	Yes