EMA/405309/2012

European Medicines Agency decision

P/0118/2012

of 2 July 2012

on the acceptance of a modification of an agreed paediatric investigation plan for tadalafil (Adcirca, Cialis) (EMEA-000452-PIP02-10-M01) 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,

Having regard to the application submitted by Eli Lilly and Company Limited on 27 February 2012 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 16 May 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 tadalafil (Adcirca, Cialis), film-coated tablet, oral suspension, oral use, gastric 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 Eli Lilly and Company Limited, Erl Wood Manor, Sunninghill Road, GU20 6PH - Windlesham, United Kingdom.

Done at London, 2 July 2012

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

EMA/405309/2012

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

EMEA-000452-PIP02-10-M01

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 22 of Regulation (EC) No 1901/2006 as amended, Eli Lilly and Company Limited submitted to the European Medicines Agency on 27 February 2012 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 application for modification proposed changes to the agreed paediatric investigation plan.

The procedure started on 19 March 2012.

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 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 annex(es) and appendix.

London, 16 May 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

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

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

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.

2. Treatment of erectile dysfunction.

   Authorised indications:

   Treatment of erectile dysfunction in adult males.

EU Number	Invented Name	Strength	Pharmaceutical form	Route of administration	Packaging	Package size
EU/1/08/476/005	Adcirca	20 mg	Film-coated tablet	Oral use	blister (alu/PVC/PE/PCTFE)	28
EU/1/08/476/006	Adcirca	20 mg	Film-coated tablet	Oral use	blister (alu/PVC/PE/PCTFE)	56

EU Number	Invented Name	Strength	Pharmaceutical form	Route of administration	Packaging	Package size
EU/1/02/237/001	Cialis	10 mg	Film-coated tablet	Oral use	blister (alu/PVC/PE/PCTFE)	4 tablets
EU/1/02/237/002	Cialis	20 mg	Film-coated tablet	Oral use	blister (alu/PVC/PE/PCTFE)	2 tablets
EU/1/02/237/003	Cialis	20 mg	Film-coated tablet	Oral use	blister (alu/PVC/PE/PCTFE)	4 tablets
EU/1/02/237/004	Cialis	20 mg	Film-coated tablet	Oral use	blister (alu/PVC/PE/PCTFE)	8 tablets
EU/1/02/237/005	Cialis	20 mg	Film-coated tablet	Oral use	blister (alu/PVC/PE/PCTFE)	12 tablets
EU/1/02/237/006	Cialis	2.5 mg	Film-coated tablet	Oral use	blister (alu/PVC/PE/PCTFE)	28 tablets
EU/1/02/237/007	Cialis	5 mg	Film-coated tablet	Oral use	blister (alu/PVC/PE/PCTFE)	14 tablets
EU/1/02/237/008	Cialis	5 mg	Film-coated tablet	Oral use	blister (alu/PVC/PE/PCTFE)	28 tablets
EU/1/02/237/009	Cialis	20 mg	Film-coated tablet	Oral use	blister (alu/PVC/PE/PCTFE)	10 tablets