EMA/409208/2014

European Medicines Agency decision

P/0187/2014

of 6 August 2014

on the acceptance of a modification of an agreed paediatric investigation plan for riociguat (ADEMPAS), (EMEA-000718-PIP01-09-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/196/2010 issued on 26 October 2010, the decision P/204/2011 issued on 26 August 2011, the decision P/0254/2012 issued on 22 October 2012, and the decision P/0293/2013 issued on 29 November 2013,

Having regard to the application submitted by Bayer Pharma AG on 24 March 2014 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 20 June 2014, 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, and to the waiver.

(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, and to the 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

Changes to the agreed paediatric investigation plan for riociguat (ADEMPAS), film-coated tablet, oral liquid, oral use, including changes to the deferral, and to the waiver, 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 Bayer Pharma AG, Müllerst. 178, 13342 – Berlin, Germany.

Done at London, 6 August 2014

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

EMA/PDCO/179643/2014 Corr

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

EMEA-000718-PIP01-09-M04

Scope of the application

Active substance(s):

Riociguat

Invented name:

ADEMPAS

Condition(s):

Treatment of pulmonary hypertension

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Film-coated tablet

Oral liquid

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Bayer Pharma AG

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, Bayer Pharma AG submitted to the European Medicines Agency on 24 March 2014 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/196/2010 issued on 26 October 2010, the decision P/204/2011 issued on 26 August 2011, the decision P/0254/2012 issued on 22 October 2012, and the decision P/0293/2013 issued on 29 November 2013.

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

The procedure started on 23 April 2014.

Scope of the modification

One clinical study has been deleted. A waiver for a new paediatric subset has been added.

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 and to the waiver in the scope set out in the Annex I of this opinion.

   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 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.

London, 20 June 2014

On behalf of the Paediatric Committee
Dr Dirk Mentzer, 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 (PIP)

1. Waiver

1.1. Condition(s): treatment of pulmonary hypertension

The waiver applies to:

- the paediatric population from birth to less than 28 days of age;
- film-coated tablet, oral liquid, oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

The waiver applies to:

- the paediatric population from 28 days to less than 6 years of age;
- film-coated tablet, oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2. Paediatric Investigation Plan

2.1. Condition: treatment of pulmonary hypertension

2.1.1. Indication(s) targeted by the PIP

Treatment of primary pulmonary arterial hypertension (PAH).

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

From 28 days to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Film-coated tablet

Oral liquid

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	Study 1: Development of an oral liquid age appropriate formulation.
Non-clinical studies	2	Study 2: 2-week repeat-dose toxicity study in juvenile rats. Study 3: 13-week repeat-dose toxicity study in juvenile rats.

Clinical studies	2	Study 5: Open-label, randomised, single dose, study to assess pharmacokinetics and investigate the relative bioavailability and food effect of the oral liquid formulation of riociguat in healthy adults. Study 6: Open-label, randomised, multicentre, multiple dose study to evaluate safety, tolerability, pharmacokinetics and efficacy of riociguat in children from 28 days to less than 18 years of age with pulmonary arterial hypertension (PAH). (Study 7 was deleted in procedure EMEA-000718-PIP01-09-M04.)
Extrapolation, modelling and simulation studies	1	Study 4: Physiologically based pharmacokinetic (PBPK) modelling study to predict the pharmacokinetic properties of riociguat in the paediatric population
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:	No
Date of completion of the paediatric investigation plan:	By December 2016
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 hypertension

Authorised indication(s):

- Chronic thromboembolic pulmonary hypertension (CTEPH)

Treatment of adult patients with WHO Functional Class (FC) II to III with inoperable CTEPH or persistent or recurrent CTEPH after surgical treatment, to improve exercise capacity.

- Pulmonary arterial hypertension (PAH)

Treatment of adult patients with pulmonary arterial hypertension (PAH) with WHO Functional Class (FC) II to III to improve exercise capacity, as monotherapy or in combination with endothelin receptor antagonists.

Efficacy has been shown in a PAH population including aetiologies of idiopathic or heritable PAH or PAH associated with connective tissue disease.

Authorised pharmaceutical form(s):

Film-coated tablet

Authorised route(s) of administration:

Oral use