EMA/693021/2013

European Medicines Agency decision

P/0293/2013

of 29 November 2013

on the refusal of a modification of an agreed paediatric investigation plan for riociguat (EMEA-000718-PIP01-09-M03) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Disclaimer

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, and the decision P/0254/2012 issued on 22 October 2012,

Having regard to the application submitted by Bayer Pharma AG on 8 July 2013 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 11 October 2013, 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 refusal of changes to the agreed paediatric investigation plan and to the waiver.

(2) It is therefore appropriate to adopt a decision on the refusal of changes to the agreed paediatric investigation plan, including changes 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, film-coated tablet, oral liquid, oral use, including changes to the waiver, 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, are hereby refused.

Article 2

This decision is addressed to Bayer Pharma AG, Müllerst. 178, 13342 – Berlin, Germany.

Done at London, 29 November 2013

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

EMA/PDCO/579761/2013

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

EMEA-000718-PIP01-09-M03

Scope of the application

Active substance(s):

Riociguat

Condition(s):

Treatment of pulmonary hypertension

Pharmaceutical form(s):

Film-coated tablet

Oral liquid

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Bayer Pharma AG

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 8 July 2013 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, and the decision P/0254/2012 issued on 22 October 2012.

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

The procedure started on 15 August 2013.

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Scope of the modification

Some measures of the Paediatric Investigation Plan have been requested to be deleted and a waiver for a new paediatric subset has been requested.

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 refuse the changes proposed by the applicant regarding the paediatric investigation plan and the scope of the waiver.

   The Norwegian Paediatric Committee member agrees 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 remain unchanged and are set out in the Annex I.

3. The scientific conclusions and the grounds for refusal are set out in the summary report appended to this opinion.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annex and appendix.

London, 11 October 2013

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

1. Waiver

1.1. Condition(s): treatment of pulmonary hypertension

The waiver applies to:

- the paediatric population from birth to less than 6 years of age;
- for 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).

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 18 years of age.

2.1.3. Pharmaceutical form(s)

Film-coated tablet.

Oral liquid.

2.1.4. Studies

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

Clinical	4	Study 4: Physiologically based pharmacokinetic (PBPK) modelling study to predict the pharmacokinetic properties of riociguat in the paediatric population 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: Open-label, uncontrolled, multicentre study to evaluate pharmacokinetics and efficacy of riociguat as add-on to inhaled nitric oxide (iNO) in neonates with persistent pulmonary hypertension of the newborn (PPHN).

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By December 2017
Deferral for one or more studies contained in the paediatric investigation plan:	Yes