EMA/662557/2012

European Medicines Agency decision

P/0254/2012

of 22 October 2012

on the acceptance of a modification of an agreed paediatric investigation plan for riociguat, (EMEA-000718-PIP01-09-M02) 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 and the decision P/204/2011 issued on 26 August 2011,

Having regard to the application submitted by Bayer Schering Pharma AG on 1 October 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 5 October 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 riociguat, film-coated tablet, oral liquid, oral 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 Bayer Schering Pharma AG, Müllerst. 178, 13342 – Berlin, Germany.

Done at London, 22 October 2012

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

EMA/PDCO/639122/2012

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

EMEA-000718-PIP01-09-M02

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 Schering Pharma AG

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Bayer Schering Pharma AG submitted to the European Medicines Agency on 1 October 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/196/2010 issued on 26 October 2010 and the decision P/204/2011 issued on 26 August 2011.

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

The procedure started on 1 October 2012.

Scope of the modification

One measure of the Paediatric Investigation Plan has been modified.

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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 and appendix.

London, 5 October 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(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