EMA/639656/2016

European Medicines Agency decision

P/0289/2016

of 4 November 2016

on the acceptance of a modification of an agreed paediatric investigation plan for riociguat (Adempas), (EMEA-000718-PIP01-09-M06) 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, the decision P/0293/2013 issued on 29 November 2013, the decision P/0187/2014 issued on 6 August 2014, and the decision P/0036/2015 issued on 6 March 2015,

Having regard to the application submitted by Bayer Pharma AG on 27 June 2016 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 September 2016, 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 (Adempas), 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 Pharma AG, Müller Strasse 178, 13353 - Berlin, Germany.

EMA/PDCO/450208/2016
London, 16 September 2016

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

EMEA-000718-PIP01-09-M06

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 27 June 2016 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, the decision P/0293/2013 issued on 29 November 2013, the decision P/0187/2014 issued on 6 August 2014, and the decision P/0036/2015 issued on 6 March 2015.

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

The procedure started on 19 July 2016.

Scope of the modification

Some measures 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 annexes and appendix.

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

Treatment of pulmonary hypertension

The waiver applies to:

- the paediatric population from birth to less than 6 years of age;
- film-coated tablet, oral liquid, oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric Investigation Plan

2.1. Condition

Treatment of pulmonary hypertension

2.1.1. Indication(s) targeted by the PIP

Treatment of pulmonary arterial hypertension (PAH)

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

From 6 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, individual dose titration study to evaluate safety, tolerability and pharmacokinetics of riociguat in children from 6 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:	Yes
Date of completion of the paediatric investigation plan:	By December 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 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