EMA/280408/2014

European Medicines Agency decision

P/0125/2014

of 16 May 2014

on the acceptance of a modification of an agreed paediatric investigation plan for entecavir (monohydrate) (Baraclude), (EMEA-000339-PIP02-09-M03) 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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on the acceptance of a modification of an agreed paediatric investigation plan for entecavir (monohydrate) (Baraclude), (EMEA-000339-PIP02-09-M03) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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/152/2010 issued on 20 August 2010, the decision P/290/2010 issued on 22 December 2010, and the decision P/0061/2014 issued on 7 March 2014,

Having regard to the application submitted by Bristol-Myers Squibb Pharma EEIG on 3 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 25 April 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.

(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.

[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 entecavir (monohydrate) (Baraclude), film-coated tablet, oral solution, oral use, including changes to the deferral, 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 Bristol-Myers Squibb Pharma EEIG, Uxbridge Bussiness Park, Sanderson Road, UB8 1DH – Uxbridge, United Kingdom.

Done at London, 16 May 2014

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

EMA/PDCO/140078/2014 Corr

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

EMEA-000339-PIP02-09-M03

Scope of the application

Active substance(s):

Entecavir (monohydrate)

Invented name:

Baraclude

Condition(s):

Treatment of chronic hepatitis B

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Film-coated tablet

Oral solution

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Bristol-Myers Squibb Pharma EEIG

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, Bristol-Myers Squibb Pharma EEIG submitted to the European Medicines Agency on 3 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/152/2010 issued on 20 August 2010, the decision P/290/2010 issued on 22 December 2010, and the decision P/0061/2014 issued on 7 March 2014.

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

The procedure started on 25 March 2014.

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 and to the deferral 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.

London, 25 April 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

1. Waiver

1.1. Condition: treatment of chronic hepatitis B

The waiver applies to:

- infants and toddlers (from birth to less than 2 years of age);
- for film-coated tablet and oral solution for oral 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 to be investigated: treatment of chronic hepatitis B

2.1.1. Indication targeted by the PIP

Treatment of chronic hepatitis B virus infection in subjects with HBeAg positive and negative compensated liver disease.

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

From 2 to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Film-coated tablets

Oral solution

2.1.4. Measures

Area	Number of studies	Description
Quality	1	**Study 1:** Development of an adequate dosing device
Non-clinical	0	Not applicable.
Clinical	2	**Study 2:** Multicentre, open-label, single arm study to evaluate the pharmacokinetics, safety, tolerability, and preliminary efficacy of entecavir in hepatitis B virus infected children and adolescents aged from 2 to less than 18 years of age **Study 3:** Randomised, double-blinded, placebo-controlled, multicentre study, to evaluate the efficacy and safety of entecavir in paediatric subjects with chronic hepatitis B infection who are HBeAg positive and nucleoside naive aged from 2 to less than 18 years

3. Follow-up, completion and deferral of PIP

Measures to address long term follow-up of potential safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By April 2013
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 chronic hepatitis B

Authorised indication(s):

- Baraclude is indicated for the treatment of chronic hepatitis B virus (HBV) infection in adults with compensated liver disease and evidence of active viral replication, persistently elevated serum alanine aminotransferase (ALT) levels and histological evidence of active inflammation and/or fibrosis. This indication is based on clinical trial data in nucleoside naive patients with HBeAg positive and HBeAg negative HBV infection. With respect to patients with lamivudine-refractory hepatitis B, see sections 4.4 and 5.1).

Authorised pharmaceutical form(s):

Film-coated tablet

Authorised route(s) of administration:

Oral use