EMA/789203/2010

European Medicines Agency decision

P/290/2010

of 22 December 2010

on the acceptance of a modification of an agreed paediatric investigation plan for entecavir (Baraclude), (EMEA-000339-PIP02-09-M01) 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 (Baraclude), (EMEA-000339-PIP02-09-M01) 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,

Having regard to the application submitted by Bristol-Myers Squibb Pharma EEIG on 1 October 2010 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 12 November 2010, 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.

(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 entecavir (Baraclude), film-coated tablet, oral solution, 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 Bristol-Myers Squibb Pharma EEIG, Uxbridge Bussiness Park, Sanderson Road, UB8 1 DH Uxbridge, United Kingdom.

Done at London, 22 December 2010

For the European Medicines Agency
Thomas Lönngren
Executive Director

(Signature on file)

EMA/PDCO/642694/2010

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

EMEA-000339-PIP02-09-M01

Scope of the application

Active substance(s):

Entecavir

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 1 October 2010 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 application for modification proposed changes to the agreed paediatric investigation plan.

The procedure started on 13 October 2010.

Scope of the modification

The modification relates to a change concerning the timelines of one of the agreed measures.

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

   The Icelandic and the Norwegian Paediatric Committee member(s) agree(s) 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(es) and appendix.

London, 12 November 2010

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: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,
- subjects with decompensated liver disease,
- subjects with lamivudine refractory chronic hepatitis B.

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. Studies

Area	Number of studies	Description
Quality	1	Study 1: Development of an adequate dosing device
Non-clinical	0	Not applicable.
Clinical	5	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

		Study 4: Single-arm, open-label study to evaluate the antiviral effect and safety of entecavir in pediatric subjects aged from 2 to less than 18 years with nucleoside-naive, HBeAg-negative compensated chronic hepatitis B infection. Study 5: Single-arm, open-label study evaluate the antiviral effect and safety of entecavir in pediatric subjects aged from 2 to less than 18 years with decompensated liver disease due to chronic hepatitis B infection Study 6: Open label study to compare entecavir used in combination, with another combination regimen in lamivudine-experienced pediatric subjects aged from 2 to less than 18 years.with chronic hepatitis B infection

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 December 2017
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 indications:

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).

EU Number	Inven-ted Name	Strength	Pharma-ceutical Form	Route Admin-istration	Pack-aging	Content (concen-tration)	Package Size
EU/1/06/343/001	Baraclude	0.5 mg	Film-coated tablet	Oral use	Bottle (HDPE)		Bottle (HDPE)
EU/1/06/343/003	Baraclude	0.5 mg	Film-coated tablet	Oral use	Blister (alu/alu)		Blister (alu/alu)
EU/1/06/343/005	Baraclude	0.05 mg/ml	Oral solution	Oral use	Bottle (HDPE)	210 ml	Bottle (HDPE)
EU/1/06/343/006	Baraclude	0.5 mg	Film-coated tablet	Oral use	Blister (alu/alu)		Blister (alu/alu)
EU/1/06/343/002	Baraclude	1 mg	Film-coated tablet	Oral use	Bottle (HDPE)		Bottle (HDPE)
EU/1/06/343/004	Baraclude	1 mg	Film-coated tablet	Oral use	Blister (alu/alu)		Blister (alu/alu)
EU/1/06/343/007	Baraclude	1 mg	Film-coated tablet	Oral use	Blister (alu/alu)		Blister (alu/alu)