EMA/192018/2013

European Medicines Agency decision

P/0082/2013

of 27 March 2013

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for 1-(2R,5R)-5-ethynyl-5-(hydroxymethyl)-2,5-dihydro-2-furanyl)-5-methyl-2,4(1H,3H)-pyrimidinedione (BMS-986001), (EMEA-001288-PIP01-12) 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 application submitted by Bristol-Myers Squibb International Corporation on 11 May 2012 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 15 March 2013, in accordance with Article 18 of Regulation (EC) No 1901/2006, and Article 21 of said Regulation and Article 13 of said Regulation,

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 agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a deferral.

(4) It is therefore appropriate to adopt a decision granting a 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

A paediatric investigation plan for 1-(2R,5R)-5-ethynyl-5-(hydroxymethyl)-2,5-dihydro-2-furanyl)-5-methyl-2,4(1H,3H)-pyrimidinedione (BMS-986001), film-coated tablet, age-appropriate solid form, oral use, 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, is hereby agreed.

Article 2

A deferral for 1-(2R,5R)-5-ethynyl-5-(hydroxymethyl)-2,5-dihydro-2-furanyl)-5-methyl-2,4(1H,3H)-pyrimidinedione (BMS-986001), film-coated tablet, age-appropriate solid form, oral use, 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, is hereby granted.

Article 3

A waiver for 1-(2R,5R)-5-ethynyl-5-(hydroxymethyl)-2,5-dihydro-2-furanyl)-5-methyl-2,4(1H,3H)-pyrimidinedione (BMS-986001), film-coated tablet, age-appropriate solid form, oral use, 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, is hereby granted.

Article 4

This decision is addressed to Bristol-Myers Squibb International Corporation, Parc de l'Alliance, Avenue de Finlande 4, 1420 - Braine-l'Alleud, Belgium.

Done at London, 27 March 2013

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

EMA/PDCO/819519/2012

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and a waiver

EMEA-001288-PIP01-12

Scope of the application

Active substance(s):

1-(2R,5R)-5-ethynyl-5-(hydroxymethyl)-2,5-dihydro-2-furanyl)-5-methyl-2,4(1H,3H)-pyrimidinedione (BMS-986001)

Condition(s):

Treatment of human immunodeficiency virus (HIV-1) infection

Pharmaceutical form(s):

Film-coated tablet

Age-appropriate solid form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Bristol-Myers Squibb International Corporation

Basis for opinion

Pursuant to Article 16 (1) of Regulation (EC) No 1901/2006 as amended, Bristol-Myers Squibb International Corporation submitted for agreement to the European Medicines Agency on 11 May 2012 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 19 June 2012.

Supplementary information was provided by the applicant on 14 December 2012. The applicant proposed modifications to the paediatric investigation plan and the request for waiver.

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Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report :

   - to agree the paediatric investigation plan in accordance with Article 18 of said Regulation,
   - to grant a deferral in accordance with Article 21 of said Regulation,
   - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

   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 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, 15 March 2013

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 human Immunodeficiency virus (HIV-1) infection

The waiver applies to:

- Children from birth to less than 15 days of age;
- For film-coated tablet, oral use;
- For Age-appropriate solid form, oral use;
- on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).

2. Paediatric Investigation Plan

2.1. Condition: Treatment of human Immunodeficiency virus (HIV-1) infection

2.1.1. Indication(s) targeted by the PIP

Treatment of HIV-1 infection in antiretroviral-naïve paediatric patients aged 15 days to less than 18 years, in combination with other antiretroviral agents.

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

From 15 days to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Film-coated tablet

Age-appropriate solid form, oral use

2.1.4. Measures

Area	Number of measures	Description
Quality	2	Measure 1 - Development of a 50-100mg film-coated tablet Measure 2 – Development of an age-appropriate solid form for oral use
Non-clinical	2	Measure 3 - Oral study of pre- and postnatal development in rats Measure 4 – Three-month oral Toxicity study in juvenile rats
Clinical	4	Measure 5 - Open-label, multicentre, multiple doses to evaluate pharmacokinetics, acceptability/palatability and safety of BMS-986001 co-administered with an Optimized Background Therapy in ARV (Anti-Retro Viral)-naive HIV-1-infected children from 6 to less than 18 years of age.

Area	Number of measures	Description
		Measure 6 - Open-label, multicentre, multiple doses to evaluate pharmacokinetics, acceptability/palatability and safety of BMS-986001 co-administered with an Optimized Background Therapy in ARV (Anti-Retro Viral)-naive HIV-1-infected children from 2 months to less than 6 years of age. Measure 7 - Open-label, single arm, multicentre trial to evaluate safety, tolerability, efficacy and pharmacokinetics of BMS-986001 co-administered with an Optimized Background Therapy in ARV (Anti-Retro Viral)-naive HIV-1-infected children from 6 to less than 18 years of age. Measure 8 - Open-label, single arm, multicentre trial to evaluate safety, tolerability, efficacy and pharmacokinetics of BMS-986001 co-administered with an Optimized Background Therapy in ARV (Anti-Retro Viral)-naive HIV-1-infected children from 15 days to 6 years of age.

2.2. Condition: Treatment of human Immunodeficiency virus (HIV-1) infection

2.2.1. Indication(s) targeted by the PIP

Treatment of HIV-1 infection in antiretroviral-experienced paediatric patients aged 2 months to less than 18 years, in combination with other antiretroviral agents.

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

From 2 months to less than 18 years of age.

2.2.3. Pharmaceutical form(s)

Film-coated tablet

Age-appropriate solid form, oral use

2.2.4. Measures

Area	Number of measures	Description
Quality	2	Measure 1 - Development of a 50-100mg film-coated tablet Measure 2 – Development of an age-appropriate solid form for oral use
Non-clinical	2	Measure 3 - Oral study of pre- and postnatal development in rats Measure 4 – Three-month oral Toxicity study in juvenile rats

Area	Number of measures	Description
Clinical	1	Measure 9 - Open-label, single arm, multicentre trial to evaluate safety, tolerability, efficacy and pharmacokinetics of BMS-986001 with an Optimized Background Therapy in ARV (Anti-retroviral)-experienced HIV-1-infected children from 2 months to less than 18 years of age.

Measures 1, 2, 3 and 4 are common to the indication “Treatment of HIV-1 infection in antiretroviral-naïve paediatric patients aged 15 days to less than 18 years, in combination with other antiretroviral agents” and have been detailed previously under Title 3.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	No.
Date of completion of the paediatric investigation plan:	By October 2022.
Deferral for one or more measures contained in the paediatric investigation plan:	Yes.