EMA/444611/2019

European Medicines Agency decision

P/0336/2019

of 10 September 2019

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for pegylated-fibroblast growth factor 21 (BMS-986036) (EMEA-002448-PIP01-18) 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 26 October 2018 under Article 16(1) of Regulation (EC) No 1901/2006,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 26 July 2019, in accordance with Article 17 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 pegylated-fibroblast growth factor 21 (BMS-986036), solution for injection, subcutaneous 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 pegylated-fibroblast growth factor 21 (BMS-986036), solution for injection, subcutaneous 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 pegylated-fibroblast growth factor 21 (BMS-986036), solution for injection , subcutaneous 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.

EMA/PDCO/248561/2019
Amsterdam, 26 July 2019

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

EMEA-002448-PIP01-18

Scope of the application

Active substance(s):

Pegylated-fibroblast growth factor 21 (BMS-986036)

Condition(s):

Treatment of non-alcoholic steatohepatitis

Pharmaceutical form(s):

Solution for injection

Route(s) of administration:

Subcutaneous 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 26 October 2018 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 4 December 2018.

Supplementary information was provided by the applicant on 12 April 2019. The applicant proposed modifications to the paediatric investigation plan.

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 17(1) 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)(b) of said Regulation, on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified subset(s) of the paediatric population and 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 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 non-alcoholic steatohepatitis (NASH)

The waiver applies to:

- the paediatric population from birth to less than 2 years;
- solution for injection, subcutaneous use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s);

  and

- the paediatric population from 2 years to less than 8 years;
- solution for injection, subcutaneous 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 non-alcoholic steatohepatitis (NASH)

2.1.1. Indication(s) targeted by the PIP

Treatment of NASH with moderate to severe liver fibrosis

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

From 8 years to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Solution for injection

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	2	**Study 1** Development of an age-appropriate presentation for dose(s) with 20 mg/mL BMS-986036 in vials for use in PIP Study 8 in patients from 8 years to less than 18 years of age with NASH with moderate to severe fibrosis.

		Study 2 Development of an age-appropriate dose(s) with 20 mg/mL (or lower concentration, if needed) BMS-986036 in vials or in prefilled syringe or prefilled pen for use in PIP Study 9 and, if appropriate, for commercialisation.
Non-clinical studies	5	**Study 3** Toxicology study in pregnant and lactating Sprague-Dawley rats (aged 10 to 11 weeks at dose initiation) and the offspring. **Study 4** Four-week, exploratory, dose-range finding, and toxicity study in juvenile rats, aged 21 days through day 50. **Study 5** Ten-week, definitive, toxicology study in juvenile rats, plus a recovery period. **Study 6** Single-dose study in adult monkeys with radiolabeled BMS-986036 **Study 7** Repeat-dose study in adult monkeys with BMS-986036 to evaluate distribution of BMS-986036 and PEG into various organs at steady-state
Clinical studies	2	**Study 8** 16-week, randomized, double-blind, placebo-controlled, parallel-group, multiple-dose study to assess the pharmacokinetics (PK), pharmacodynamics (PD), initial safety, and tolerability of BMS-986036 in children and adolescent patients from 8 years to less than 18 years of age with NASH with moderate to severe fibrosis. **Study 9** 48-week, double-blind, placebo-controlled study to assess the safety and efficacy of BMS-986036 in children and adolescent subjects from 8 years to less than 18 years of age with NASH with moderate to severe fibrosis.
Extrapolation, modelling and simulation studies	0	Not applicable
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 October 2029
Deferral for one or more measures contained in the paediatric investigation plan:	Yes