EMA/173738/2019

European Medicines Agency decision

P/0110/2019

of 22 March 2019

on the agreement of a paediatric investigation plan and on the granting of a deferral for N-hydroxy-5-methylfuran-2-sulfonamide (BMS-986231) (EMEA-002378-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 22 May 2018 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 1 March 2019, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 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.

(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.

[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 N-hydroxy-5-methylfuran-2-sulfonamide (BMS-986231), powder for concentrate for solution for infusion, age-appropriate dosage form for parenteral use, intravenous 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 N-hydroxy-5-methylfuran-2-sulfonamide (BMS-986231), powder for concentrate for solution for infusion, age-appropriate dosage form for parenteral use, intravenous 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

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/837719/2018
London, 1 March 2019

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

EMEA-002378-PIP01-18

Scope of the application

Active substance(s):

N-hydroxy-5-methylfuran-2-sulfonamide (BMS-986231)

Condition(s):

Treatment of acute heart failure

Pharmaceutical form(s):

Powder for concentrate for solution for infusion

Age-appropriate dosage form for parenteral use

Route(s) of administration:

Intravenous 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 22 May 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 26 June 2018.

Supplementary information was provided by the applicant on 26 November 2018. The applicant proposed modifications to the paediatric investigation plan and withdrew its request for a 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 17(1) of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation.

   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 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

Not applicable.

2. Paediatric investigation plan

2.1. Condition

Treatment of acute heart failure

2.1.1. Indication(s) targeted by the PIP

Short-term treatment of paediatric patients with acute heart failure, including patients with low cardiac output states following cardiac surgery

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

From birth to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Powder for concentrate for solution for infusion

Age-appropriate dosage form for parenteral use

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of lower strength of powder for concentrate for solution for infusion appropriate for young children
Non-clinical studies	2	**Study 2** Exploratory study in neonatal dogs to evaluate toxicokinetics (TK), mortality, tolerability and feasibility of micro infusion pump dosing **Study 3** Definitive toxicity study in neonatal dogs to evaluate mortality, toxicity and systemic exposure, TK, serum chemistry, urinalysis, organ weights, gross and microscopic pathology
Clinical studies	2	**Study 4** Double-blind, randomised, placebo-controlled trial to evaluate pharmacokinetics (PK), safety and tolerability of BMS-986231 as add-on to best standard of care: • Part A in children from 6 to less than 18 years of age with acute heart failure (AHF) due to dilated cardiomyopathy (DCM)

		• Part B: in children from birth to less than 6 years of age with congenital heart disease (CHD) after surgery with cardio-pulmonary bypass (CPB) **Study 5** Double-blind, randomised, placebo-controlled trial to evaluate safety and efficacy of BMS-986231 in terms of superiority over placebo as add-on to best standard of care in children from birth to less than 18 years of age with congenital heart disease (CHD) after surgery with cardio-pulmonary bypass (CPB)
Extrapolation, modelling and simulation studies	1	**Study 6** Population PK and PK/PD non-linear mixed effects models to evaluate the use of BMS-986231 in children from 6 to less than 18 years of age with acute heart failure (AHF) due to dilated cardiomyopathy (DCM)
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:	No
Date of completion of the paediatric investigation plan:	By October 2028
Deferral for one or more measures contained in the paediatric investigation plan:	Yes