

EMA/565682/2017

European Medicines Agency decision

P/0283/2017

of 4 October 2017

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for (Z)-N-(3-bromo-4-fluorophenyl)-N'-hydroxy-4-(2-(sulfamoylamino)ethylamino)-1,2,5-oxadiazole-3-carboximidamide (EMEA-002072-PIP01-16) 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 726/2004¹,

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 Agency²,

Having regard to the application submitted by Incyte Corporation on 28 November 2016 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 18 August 2017, 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 (Z)-N-(3-bromo-4-fluorophenyl)-N'-hydroxy-4-(2-(sulfamoylamino)ethylamino)-1,2,5-oxadiazole-3-carboximidamide, tablet, age appropriate oral formulation, 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 (Z)-N-(3-bromo-4-fluorophenyl)-N'-hydroxy-4-(2-(sulfamoylamino)ethylamino)-1,2,5-oxadiazole-3-carboximidamide, tablet, age appropriate oral formulation, 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 (Z)-N-(3-bromo-4-fluorophenyl)-N'-hydroxy-4-(2-(sulfamoylamino)ethylamino)-1,2,5-oxadiazole-3-carboximidamide, tablet, age appropriate oral formulation, 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 Incyte Corporation, 1801 Augustine Cut-Off, DE 19803 – Wilmington, United States.

EMA/PDCO/353822/2017
London, 18 August 2017

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

EMA-002072-PIP01-16

Scope of the application

Active substance(s):

(Z)-N-(3-bromo-4-fluorophenyl)-N'-hydroxy-4-(2-(sulfamoylamino)ethylamino)-1,2,5-oxadiazole-3-carboximidamide

Condition(s):

Treatment of all conditions included in the category of malignant neoplasms including Hodgkin lymphoma (except nervous system, haematopoietic and lymphoid tissue other than Hodgkin lymphoma)

Pharmaceutical form(s):

Tablet

Age appropriate oral formulation

Route(s) of administration:

Oral use

Name / corporate name of the PIP applicant:

Incyte Corporation

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Incyte Corporation submitted for agreement to the European Medicines Agency on 28 November 2016 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 3 January 2017.

Supplementary information was provided by the applicant on 25 May 2017. 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 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 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 all conditions included in the category of malignant neoplasms including Hodgkin lymphoma (except nervous system, haematopoietic and lymphoid tissue other than Hodgkin lymphoma)

The waiver applies to:

- the paediatric population from birth to less than 6 months;
- tablet, age-appropriate oral formulation, oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

2. Paediatric investigation plan

2.1. Condition

Treatment of all conditions included in the category of malignant neoplasms including Hodgkin lymphoma (except nervous system, haematopoietic and lymphoid tissue other than Hodgkin lymphoma)

2.1.1. Indication(s) targeted by the PIP

Treatment of select unresectable or metastatic solid tumours with epacadostat in combination with pembrolizumab in paediatric patients between the ages of 6 months and 18 years of age

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

From 6 months to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Tablet

Age-appropriate oral formulation

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	2	Study 1 To modify the current adult formulation epacadostat tablets at the point of administration for young children unable to swallow whole tablets to allow initiation of the clinical trial prior to availability of age appropriate formulation.

Area	Number of measures	Description
		Study 2 Development of an age-appropriate oral liquid dosage form.
Non-clinical studies	1	Study 3 Non-clinical biomarker study in paediatric tumour tissue.
Clinical studies	2	Study 4 Open-label dose escalation study to evaluate safety and tolerability, pharmacokinetics (PK), pharmacodynamics, and anti-cancer activity of epacadostat in combination with pembrolizumab in patients 6 months to less than 18 years of age with any refractory or relapsed solid tumour for which no effective treatment is available and an expansion phase in children from 6 months to less than 18 years of age with tumours known to be responsive to anti-PD-1 therapy or where RNA-seq analysis suggests a high likelihood of response to combination immunotherapy. Study 5 Randomised, controlled study to evaluate efficacy, safety, and PK of epacadostat in combination with pembrolizumab compared to standard anti-cancer care in patients 6 months to less than 18 years of age with a paediatric solid malignant tumour type determined based on results of Study 3.
Extrapolation, modelling and simulation studies	1	Study 6 PK/PD Modelling and Simulation study to characterize exposure-response relationship and for dose selection of epacadostat in combination with pembrolizumab in children from 6 months to less than 18 years of age.
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 January 2027
Deferral for one or more measures contained in the paediatric investigation plan:	Yes