EMA/469681/2018

European Medicines Agency decision

P/0246/2018

of 15 August 2018

on the acceptance of a modification of an agreed paediatric investigation plan for (Z)-N-(3-bromo-4-fluorophenyl)-N'-hydroxy-4-(2-(sulfamoylamino)ethylamino)-1,2,5-oxadiazole-3-carboximidamide (EMEA-002072-PIP01-16-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.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Contact EMA www.ema.europa.eu/contact

European Medicines Agency decision

P/0246/2018

of 15 August 2018

on the acceptance of a modification of an agreed paediatric investigation plan for (Z)-N-(3-bromo-4-fluorophenyl)-N'-hydroxy-4-(2-(sulfamoylamino)ethylamino)-1,2,5-oxadiazole-3-carboximidamide (EMEA-002072-PIP01-16-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/0283/2017 issued on 4 October 2017,

Having regard to the application submitted by Incyte Corporation on 22 March 2018 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 29 June 2018, 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 plan.

(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 (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, 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 Incyte Corporation, 1801 Augustine Cut-Off, DE 19803 – Wilmington, United States.

EMA/PDCO/195557/2018
London, 29 June 2018

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

EMEA-002072-PIP01-16-M01

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 22 of Regulation (EC) No 1901/2006 as amended, Incyte Corporation submitted to the European Medicines Agency on 22 March 2018 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/0283/2017 issued on 4 October 2017.

The application for modification proposed changes to the agreed paediatric investigation plan.

The procedure started on 2 May 2018.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified.

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 in the scope set out in the Annex I of this opinion.

   The Norwegian Paediatric Committee member agrees 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 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 than18 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. (INCB 24360-2XX) **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 than18 years of age with a paediatric solid malignant tumour type determined based on results of Study 3. (INCB 24360-3XX)
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