EMA/775595/2018

European Medicines Agency decision

P/0393/2018

of 6 December 2018

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for evobrutinib (EMEA-002284-PIP01-17) 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

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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 Merck KGaA on 15 December 2017 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 19 October 2018, 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 evobrutinib, film-coated tablet, age-appropriate oral solid dosage 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 evobrutinib, film-coated tablet, age-appropriate oral solid dosage 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 evobrutinib, film-coated tablet, age-appropriate oral solid dosage 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 Merck KGaA, Frankfurter Str. 250, 64293 – Darmstadt, Germany.

EMA/PDCO/535284/2018 Corr
London, 19 October 2018

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

EMEA-002284-PIP01-17

Scope of the application

Active substance(s):

Evobrutinib

Condition(s):

Treatment of multiple sclerosis

Pharmaceutical form(s):

Film-coated tablet

Age-appropriate oral solid dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Merck KGaA

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Merck KGaA submitted for agreement to the European Medicines Agency on 15 December 2017 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulationand a waiver under Article 13 of said Regulation.

The procedure started on 23 January 2018.

Supplementary information was provided by the applicant on 13 July 2018. 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)(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 multiple sclerosis

The waiver applies to:

- the paediatric population from birth to less than 10 years of age;
- film-coated tablet, age-appropriate oral solid dosage form, oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies are not feasible.

2. Paediatric investigation plan

2.1. Condition:

Treatment of multiple sclerosis

2.1.1. Indication(s) targeted by the PIP

Treatment of relapsing remitting multiple sclerosis

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

From 10 to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Film-coated tablet

Age-appropriate oral solid dosage form

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1:** Development of minitablets of a size and strength suitable for administration to children unable to swallow tablets
Non-clinical studies	0	Not applicable
Clinical studies	1	**Study 2:** Open-label, single dose study to determine the PK, PD and preliminary safety profile of evobrutinib in children and adolescents with relapsing remitting multiple sclerosis (RRMS); followed by a randomised, double

		blind, double-dummy, active controlled phase to compare the safety and efficacy of evobrutinib with IFNβ-1a for treating children and adolescents with RRMS
Extrapolation, modelling and simulation studies	1	**Study 3:** Population PK/PD and exposure response model for study optimisation
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 June 2028
Deferral for one or more measures contained in the paediatric investigation plan:	Yes