EMA/125284/2018

European Medicines Agency decision

P/0061/2018

of 16 March 2018

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for ruxolitinib (phosphate) (Jakavi), (EMEA-000901-PIP04-17) 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 Novartis Europharm Limited on 19 October 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 26 January 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 ruxolitinib (phosphate) (Jakavi), tablet, age-appropriate oral dosage form, oral use, gastric 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 ruxolitinib (phosphate) (Jakavi), tablet, age-appropriate oral dosage form, oral use, gastric 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 ruxolitinib (phosphate) (Jakavi), tablet, age-appropriate oral dosage form, oral use, gastric 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 covers all conditions, indications, pharmaceutical forms, routes of administration, measures, timelines, waivers and deferrals, as agreed in the decision P/175/2010 issued on 20 September 2010 and P/176/2010 issued on 20 September 2010, including subsequent modifications thereof.

Article 5

This decision is addressed to Novartis Europharm Limited, Frimley Business Park, GU167SR – Camberley, United Kingdom.

EMA/PDCO/831140/2017
London, 26 January 2018

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

EMEA-000901-PIP04-17

Scope of the application

Active substance(s):

Ruxolitinib (phosphate)

Invented name:

Jakavi

Condition(s):

Treatment of chronic Graft versus Host Disease (cGvHD)

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Tablet

Age-appropriate oral dosage form

Route(s) of administration:

Oral use

Gastric use

Name/corporate name of the PIP applicant:

Novartis Europharm Limited

Information about the authorised medicinal product:

See Annex II

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5510
Send a question via our website www.ema.europa.eu/contact

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Novartis Europharm Limited submitted for agreement to the European Medicines Agency on 19 October 2017 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 28 November 2017.

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.

   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 annexes 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 chronic Graft versus Host Disease (cGvHD)

The waiver applies to:

- newborn infants (from birth to less than 28 days);
- tablet, age-appropriate oral dosage form, oral use, gastric 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).

2. Paediatric investigation plan

2.1. Condition:

Treatment of chronic Graft versus Host Disease (cGvHD)

2.1.1. Indication(s) targeted by the PIP

Treatment of chronic Graft versus Host Disease (cGvHD) after allogeneic haematopoietic stem cell transplantation (HSCT).

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

From 28 days to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Tablet

Age-appropriate oral dosage form

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1:** Development of an age-appropriate oral dosage form *This study is the same as study 1 of the ruxolitinib PIP EMEA-000901-PIP03-16 and subsequent modifications thereof*
Non-clinical studies	1	**Study 2:** Definitive juvenile toxicity study in rats *This study is the same as study 2 of the ruxolitinib PIP EMEA-000901-PIP03-16 and subsequent modifications thereof*

Clinical studies	2	**Study 3:** Open-label, randomised, active-controlled trial to evaluate pharmacokinetics, safety and efficacy of ruxolitinib compared to best available therapy (BAT) in adults and adolescents from 12 to less than 18 years of age with corticosteroid-refractory (SR) cGvHD following allogeneic HSCT (INC424 D2301) **Study 4:** Open-label uncontrolled trial to evaluate pharmacokinetics, safety and activity of ruxolitinib in children from 28 days to less than 18 years of age with moderate or severe treatment-naïve or SR-cGvHD following allogeneic HSCT (INC424G12201)
Extrapolation, modelling and simulation studies	3	**Study 5:** Population PK (PopPK) modelling and simulation study to support the use of ruxolitinib for the treatment of cGvHD in children from 28 days to less than 18 years of age with treatment-naïve or SR-cGvHD following allogeneic HSCT **Study 6:** Physiologically-based PK (PBPK) modelling and simulation study to support the use of ruxolitinib for the treatment of cGvHD in children from 28 days to less than 18 years of age with treatment-naïve or SR-cGvHD following allogeneic HSCT **Study 7:** Extrapolation study to support the use of ruxolitinib for the treatment of cGvHD in children from 28 days to less than 18 years of age with treatment-naïve or SR-cGvHD following allogeneic HSCT
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 2025
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Treatment of myelofibrosis

Authorised indication(s):

Jakavi is indicated for the treatment of disease-related splenomegaly or symptoms in adult patients with primary myelofibrosis (also known as chronic idiopathic myelofibrosis), post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis.

2. Treatment of polycythaemia vera

Authorised indication(s):

Jakavi is indicated for the treatment of adult patients with polycythaemia vera who are resistant to or intolerant of hydroxyurea.

Authorised pharmaceutical form(s):

Tablet

Authorised route(s) of administration:

Oral use