EMA/197383/2021

European Medicines Agency decision

P/0172/2021

of 9 April 2021

on the acceptance of a modification of an agreed paediatric investigation plan for ruxolitinib (phosphate) (Jakavi), (EMEA-000901-PIP03-16-M02) 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 European Medicines Agency's decision P/0349/2017 issued on 1 December 2017 and the decision P/0190/2019 issued on 15 May 2019,

Having regard to the application submitted by Novartis Europharm Limited on 17 December 2020 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 26 March 2021, 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 ruxolitinib (phosphate) (Jakavi), tablet, age-appropriate oral dosage form, oral use, gastric 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 covers all conditions, indications, pharmaceutical forms, routes of administration, measures, timelines, waivers and deferrals, as agreed in the decision P/0061/2018 issued on 16 March 2018, including subsequent modifications thereof.

Article 3

This decision is addressed to Novartis Europharm Limited, Vista Building, Elm Park, Merrion Road, D04 A9N6 – Dublin, Ireland.

EMA/PDCO/21321/2021
Amsterdam, 26 March 2021

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

EMEA-000901-PIP03-16-M02

Scope of the application

Active substance(s):

Ruxolitinib (phosphate)

Invented name:

Jakavi

Condition(s):

Treatment of acute Graft versus Host Disease

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

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Novartis Europharm Limited submitted to the European Medicines Agency on 17 December 2020 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/0349/2017 issued on 1 December 2017 and the decision P/0190/2019 issued on 15 May 2019.

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

The procedure started on 26 January 2021.

Scope of the modification

Some measures 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 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 acute Graft versus Host Disease (aGvHD)

The waiver applies to:

- newborn infants (from birth to less than 28 days);
- tablet and age-appropriate oral dosage form, oral use and 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 acute Graft versus Host Disease (aGvHD)

2.1.1. Indication(s) targeted by the PIP

Treatment of acute Graft versus Host Disease (aGvHD) 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
Non-clinical studies	1	**Study 2** Definitive juvenile toxicity study in rats
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) aGvHD following allogeneic HSCT (INC424C2301)

		Study 4 Two-part study in children from 28 days to less than 18 years of age with treatment-naïve or SR-aGvHD following allogeneic HSCT, with an open-label uncontrolled Part I to evaluate pharmacokinetics and safety of ruxolitinib, and an open-label uncontrolled Part II to evaluate safety and activity of ruxolitinib (INC424F12201)
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 aGvHD in children from 28 days to less than 18 years of age with treatment-naïve or SR-aGvHD following allogeneic HSCT **Study 6** Physiologically-based PK (PBPK) modelling and simulation study to support the use of ruxolitinib for the treatment of aGvHD in children from 28 days to less than 18 years of age with treatment-naïve or SR-aGvHD following allogeneic HSCT **Study 7** Extrapolation study to support the use of ruxolitinib for the treatment of aGvHD in children from 28 days to less than 18 years of age with treatment-naïve or SR-aGvHD 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 December 2023
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