EMA/517231/2018

European Medicines Agency decision

P/0275/2018

of 31 August 2018

on the acceptance of a modification of an agreed paediatric investigation plan for tofacitinib (Xeljanz) (EMEA-000576-PIP03-12-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.

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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/0195/2014 issued on 8 August 2014,

Having regard to the application submitted by Pfizer Limited on 4 May 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 27 July 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 and to the deferral and to the waiver.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, including changes to the deferral and to the 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

Changes to the agreed paediatric investigation plan for tofacitinib (Xeljanz), film-coated tablet, oral solution, oral use, including changes to the deferral and to the waiver, 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 4

This decision covers all conditions, indications, pharmaceutical forms, routes of administration, measures, timelines, waivers and deferrals, as agreed in the decision P/144/2010 issued on 30 July 2010, including subsequent modifications thereof.

Article 2

This decision is addressed to Pfizer Limited, Ramsgate Road, CT13 - 9NJ Sandwich, Kent, United Kingdom.

EMA/PDCO/293995/2018 Corr
London, 27 July 2018

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

EMEA-000576-PIP03-12-M01

Scope of the application

Active substance(s):

Tofacitinib

Invented name:

Xeljanz

Condition(s):

Treatment of ulcerative colitis

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Film-coated tablet

Oral solution

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Pfizer 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, Pfizer Limited submitted to the European Medicines Agency on 4 May 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/0195/2014 issued on 8 August 2014.

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

The procedure started on 29 May 2018.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified. A waiver for a new paediatric subset has been added.

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 and to the deferral and to the waiver 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 ulcerative colitis

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- for film-coated tablet and oral solution, oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric investigation plan

2.1. Condition:

Treatment of ulcerative colitis

2.1.1. Indication(s) targeted by the PIP

Treatment of children and adolescents from 2 to less than 18 years of age with moderate to severe ulcerative colitis, who have had an inadequate response or been intolerant to prior therapy with corticosteroids, azathioprine/6-mercaptopurine, anti-TNF alpha agent, or have medical contraindications to such therapies

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

From 2 to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Film-coated tablet

Oral solution

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of oral solution 1 mg/ml

Non-clinical studies	3	**Study 2** 39 week toxicology study in juvenile non-human primates followed by 26 week recovery period **Study 3** 1 month toxicity study in juvenile rats followed by 2 months recovery **Study 4** Fertility study in juvenile rats for 50 days in males and 35 days in females
Clinical studies	1	**Study 5** PK, efficacy and safety trial with an open–label induction phase followed by a placebo–controlled maintenance phase to evaluate PK, safety, efficacy and tolerability of tofacitinib for induction and maintenance of remission in children from 2 to less than 18 years of age with ulcerative colitis *Induction Phase:* Part 1: Determination of PK in 20 children from 12 to less than 18 years of age prior to enrolment of younger patients Part 2: Enrolment of children from 2 to less than 18 years of age when doses are determined based on results of study 6 and Part 1 *Maintenance Phase:* Following the open–label induction phase, subjects who complete induction and achieve clinical response or clinical remission must be offered to continue in the maintenance phase of the study
Extrapolation, modelling and simulation studies	1	**Study 6** Modelling and simulation study to select doses for evaluating the use of tofacitinib in children from 2 to less than 18 years of age with ulcerative colitis
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 April 2022
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 rheumatoid arthritis

Authorised indication(s):

- XELJANZ in combination with methotrexate (MTX) is indicated for the treatment of moderate to severe active rheumatoid arthritis (RA) in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying antirheumatic drugs. XELJANZ can be given as monotherapy in case of intolerance to MTX or when treatment with MTX is inappropriate.

Authorised pharmaceutical form(s):

Film-coated tablet

Authorised route(s) of administration:

Oral use