EMA/392211/2014

European Medicines Agency decision

P/0195/2014

of 8 August 2014

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for tofacitinib (EMEA-000576-PIP03-12) 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 Pfizer Limited on 14 February 2013 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 20 June 2014, in accordance with Article 18 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 tofacitinib, film-coated tablet, oral solution, 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 tofacitinib, film-coated tablet, oral solution, 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 tofacitinib, film-coated tablet, oral solution, 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 Pfizer Limited, Ramsgate Road, CT13 9NJ - Sandwich, Kent, United Kingdom.

Done at London, 8 August 2014

For the European Medicines Agency
Guido Rasi
Executive Director
(Signature on file)

EMA/PDCO/196287/2014

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

EMEA-000576-PIP03-12

Scope of the application

Active substance(s):

Tofacitinib

Condition(s):

Treatment of ulcerative colitis

Pharmaceutical form(s):

Film-coated tablet

Oral solution

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Pfizer Limited

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Pfizer Limited submitted for agreement to the European Medicines Agency on 14 February 2013 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 20 March 2013.

Supplementary information was provided by the applicant on 31 March 2014. The applicant proposed modifications to the paediatric investigation plan.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7040
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

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 18 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)(a) of said Regulation, on the grounds that the specific medicinal product is likely to be ineffective or unsafe in part or all of the paediatric population.

   The Icelandic and the Norwegian Paediatric Committee members agree 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.

London, 20 June 2014

On behalf of the Paediatric Committee
Dr Dirk Mentzer, Chairman
(Signature on file)

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 4 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 4 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 4 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 4 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 4 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 4 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 March 2021
Deferral for one or more measures contained in the paediatric investigation plan:	Yes