EMADOC-1700519818-2035701

European Medicines Agency decision

EMA/PE/0000226763

of 14 April 2025

on the acceptance of a modification of an agreed paediatric investigation plan for tofacitinib citrate (XELJANZ) 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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on the acceptance of a modification of an agreed paediatric investigation plan for tofacitinib citrate (XELJANZ) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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 Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0439/2022 issued on 28 October 2022, the decision P/0195/2014 issued on 8 August 2014, the decision P/0275/2018 issued on 31 August 2018, the decision P/0071/2019 issued on 22 March 2019, the decision P/0165/2020 issued on 24 April 2020, the decision P/0380/2020 issued on 9 September 2020, and the decision P/0009/2021 issued on 15 January 2021,

Having regard to the application submitted by Pfizer Europe MA EEIG on 25 November 2024 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 28 February 2025, 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.

(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.

[1] OJ L 378, 27.12.2006, p.1, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for tofacitinib citrate (XELJANZ), including changes to the deferral, 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/144/2010 issued on 30 July 2010, including subsequent modifications thereof.

Article 3

This decision is addressed to Pfizer Europe MA EEIG, Boulevard De La Plaine 17, 1050 - Brussels, Brussels-Capital Region, Belgium.

EMADOC-1700519818-1803164 Corr[1]

Amsterdam, 28 February 2025

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

EMA/PE/0000226763

Scope of the application

Active substance(s):

Tofacitinib (citrate)

Invented name and authorisation status:

See Annex II

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 Europe MA EEIG

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Pfizer Europe MA EEIG submitted to the European Medicines Agency on 25 November 2024 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/0439/2022 issued on 28 October 2022, the decision P/0195/2014 issued on 8 August 2014, the decision P/0275/2018 issued on 31 August 2018, the decision P/0071/2019 issued on 22 March 2019, the decision P/0165/2020 issued on 24 April 2020, the decision P/0380/2020 issued

[1] 10 April 2025 page 2 decision references corrected under

on 9 September 2020, the decision P/0009/2021 issued on 15 January 2021 and the decision P/0439/2022 issued on 28 October 2022.

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

The procedure started on 2 January 2025.

Scope of the modification

Some measures and timelines 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 and to the deferral in the scope set out in the Annex I of this opinion.

   The Paediatric Committee member of Norway 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;
- film-coated tablet, oral solution, oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

1. Paediatric investigation plan

1.1. Condition:

Treatment of ulcerative colitis

1.1.1. Indication(s) targeted by the PIP

Treatment of children and adolescents from 2 to less than 18 years of age with moderately to severely active ulcerative colitis, who have had an inadequate response, lost response or were intolerant to either conventional therapy or a biological agent

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

From 2 years to less than 18 years of age

1.1.3. Pharmaceutical form(s)

Film-coated tablet

Oral solution

1.1.4. Measures

Area	Description
Quality-related studies	**Study 1** Development of oral solution 1 mg/ml **Study 7 Study deleted in procedure EMEA-000576-PIP03-12-M06** **Study 8 Study deleted in procedure EMEA-000576-PIP03-12-M06**
Non-clinical studies	**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	**Study 5 (A3921210)** Open-label, PK, efficacy and safety trial with an open-label extension phase, to evaluate PK, safety, efficacy and tolerability of tofacitinib in children from 2 to less than 18 years of age with moderately to severely active ulcerative colitis
Extrapolation, modelling and simulation studies	**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 **Study 9 Study deleted in procedure EMEA-000576-PIP03-12-M06** **Study 10** Population PK analysis using data from the PK, efficacy and safety study in paediatric UC patients **Study 11 Study deleted in procedure EMEA-000576-PIP03-12-M06**
Other studies	Not applicable.
Other measures	Not applicable.

2. 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 2027
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

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.
  - Invented name(s): Xeljanz
  - Authorised pharmaceutical form(s): Film-coated tablet, prolonged-release tablets, oral solution
  - Authorised route(s) of administration: Oral use
  - Authorised via centralised procedure

2. Treatment of psoriatic arthritis

Authorised indication(s):

- Tofacitinib in combination with MTX is indicated for the treatment of active psoriatic arthritis (PsA) in adult patients who have had an inadequate response or who have been intolerant to a prior disease-modifying antirheumatic drug (DMARD) therapy.
  - Invented name(s): Xeljanz
  - Authorised pharmaceutical form(s): Film-coated tablet, prolonged-release tablets
  - Authorised route(s) of administration: Oral use
  - Authorised via centralised procedure

3. Treatment of ankylosing spondylitis

Authorised indication(s):

- Tofacitinib is indicated for the treatment of adult patients with active ankylosing spondylitis (AS) who have responded inadequately to conventional therapy
  - Invented name(s): Xeljanz
  - Authorised pharmaceutical form(s): Film-coated tablet, prolonged-release tablets
  - Authorised route(s) of administration: Oral use
  - Authorised via centralised procedure

4. Treatment of ulcerative colitis

Authorised indication(s):

- Tofacitinib is indicated for the treatment of adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic agent.
  - Invented name(s): Xeljanz

- Authorised pharmaceutical form(s): Film-coated tablet
- Authorised route(s) of administration: Oral use
- Authorised via centralised procedure

5. Treatment of juvenile idiopathic arthritis

Authorised indication(s):

- Tofacitinib is indicated for the treatment of active polyarticular juvenile idiopathic arthritis (rheumatoid factor positive [RF+] or negative [RF-] polyarthritis and extended oligoarthritis), and juvenile psoriatic arthritis (PsA) in patients 2 years of age and older, who have responded inadequately to previous therapy with DMARDs.

  Tofacitinib can be given in combination with methotrexate (MTX) or as monotherapy in case of intolerance to MTX or where continued treatment with MTX is inappropriate

  - Invented name(s): Xeljanz
  - Authorised pharmaceutical form(s): Film-coated tablet, oral solution
  - Authorised route(s) of administration: Oral use
  - Authorised via centralised procedure