EMADOC-1700519818-1840302

European Medicines Agency decision

EMA/PE/0000222532

of 28 January 2025

on the acceptance of a modification of an agreed paediatric investigation plan for tofacitinib (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 (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/144/2010 issued on 30 July 2010, the decision P/162/2011 issued on 4 July 2011, the decision P/0064/2012 issued on 28 March 2012, the decision P/0169/2013 issued on 30 July 2013, the decision P/0035/2014 issued on 5 March 2014, the decision P/0013/2015 issued on 30 January 2015, the decision P/0054/2017 issued on 17 March 2017, the decision P/0296/2017 issued on 4 October 2017, the decision P/0035/2018 issued on 30 January 2018, the decision P/0203/2018 issued on 17 July 2018, the decision P/0134/2019 issued on 17 April 2019, the decision P/0227/2020 issued on 17 June 2020, the decision P/0102/2023 issued on 24 March 2023 and the decision P/0308/2023 issued on 7 August 2023, and the decision P/0239/2024 issued on 18 July 2024,

Having regard to the application submitted by Pfizer Europe MA EEIG on 6 September 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 13 December 2024, 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, 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 (Xeljanz), 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 is addressed to Pfizer Europe MA EEIG, Boulevard De La Plaine 17, Brussels – 1050, Belgium.

EMADOC-1700519818-1693737
Amsterdam, 13 December 2024

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

EMA/PE/0000222532

Scope of the application

Active substance(s):

Tofacitinib

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis)

Pharmaceutical form(s):

Film-coated tablet

Prolonged-release film-coated tablet

Age-appropriate oral liquid formulation

Prolonged-release age-appropriate oral formulation

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 6 September 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/144/2010 issued on 30 July 2010, the decision P/162/2011 issued on 4 July 2011, the decision P/0064/2012 issued on 28 March 2012, the decision P/0169/2013 issued on 30 July 2013,

the decision P/0035/2014 issued on 5 March 2014, the decision P/0013/2015 issued on 30 January 2015, the decision P/0054/2017 issued on 17 March 2017, the decision P/0296/2017 issued on 4 October 2017, the decision P/0035/2018 issued on 30 January 2018, the decision P/0203/2018 issued on 17 July 2018, the decision P/0134/2019 issued on 17 April 2019, the decision P/0227/2020 issued on 17 June 2020, the decision P/0102/2023 issued on 24 March 2023 and the decision P/0308/2023 issued on 7 August 2023, and the decision P/0239/2024 issued on 18 July 2024.

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

The procedure started on 14 October 2024.

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 in the scope set out in the Annex I of this opinion.

   The Paediatric Committee members of Liechtenstein and Norway agree 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 chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis)

The waiver applies to:

- children from birth to less than 2 years;
- film-coated tablet, prolonged-release film-coated tablet, age-appropriate oral liquid formulation, prolonged-release age-appropriate oral formulation, oral 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 idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis)

2.1.1. Indication targeted by the PIP

Treatment of juvenile idiopathic arthritis (extended oligoarthritis, RF+ polyarthritis, RF- polyarthritis, enthesitis related arthritis, psoriatic arthritis, systemic JIA)

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

From 2 years to less than 18 years of age

2.1.3. Pharmaceutical form

Film-coated tablet

Prolonged-release film-coated tablet

Age-appropriate oral liquid formulation

Prolonged-release age-appropriate oral formulation

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1** Development of age appropriate oral liquid formulation **Study 12** Development of prolonged-release film-coated tablet

	Study 13 Development of prolonged-release age-appropriate oral formulation(s), suitable for children from 2 to less than 12 years of age
Non-clinical studies	**Study 2** Juvenile non-human primate 39-week toxicology study followed by 26-week recovery period **Study 3** Juvenile rat 1-month toxicity study followed by 2-month recovery **Study 4** Juvenile rat fertility study for 50 days in males and 35 days in females
Clinical studies	**Study 5 (A3921103)** Open label, non-randomised, multiple dose pharmacokinetic study in children from 2 to less than 18 years of age with juvenile idiopathic arthritis (JIA) **Study 6 (A3921104)** Randomised, withdrawal, double-blind, placebo-controlled study to evaluate efficacy and safety of tofacitinib in children from 2 to less than 18 years of age with polyarticular course juvenile idiopathic arthritis (i.e. extended oligoarthritis, RF+/RF- polyarthritis and systemic arthritis without systemic features), enthesitis related arthritis and psoriatic arthritis **Study 7 (A3921165)** Randomised, double-blind, placebo-controlled withdrawal study to evaluate efficacy, safety and tolerability of tofacitinib in children from 2 to less than 18 years of age with systemic juvenile idiopathic arthritis with or without active systemic features **Study 8** Single-dose study to evaluate pharmacokinetics of tofacitinib prolonged-release age-appropriate oral formulation in children from 2 to less than 12 years of age with juvenile idiopathic arthritis.
Extrapolation, modelling and simulation studies	**Study 9** Study to bridge efficacy and safety from tofacitinib film-coated tablet formulation to the prolonged-release film-coated tablet formulation in adult patients with rheumatoid arthritis

	Study 10 Population PK analysis using data from the multiple dose PK study (A3921103) and safety and efficacy studies (A3921104, A3921165) in paediatric patients with juvenile idiopathic arthritis **Study 11** Study to bridge efficacy and safety from tofacitinib film-coated formulation to the prolonged-release formulation(s) in paediatric patients with juvenile idiopathic arthritis
Other studies	Not applicable
Other measures	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 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):

- Tofacitinib 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. Tofacitinib 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, oral solution, prolonged-release tablets
  - Authorised route(s) of administration: Oral use
  - Authorised via centralised procedure

2. Treatment of Psoriatic arthritis:

- 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

- 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:

- 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

- 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