MHRA
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Canary Wharf
London
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United Kingdom

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Decision Cover Letter

Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan and to the deferral.

MHRA-101767-PIP01-24-M01

Scope of the Application

Active Substance(s)

TOFACITINIB CITRATE

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 Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Pfizer Limited submitted to the licensing authority on 23/12/2024 08:37 GMT an application for a Modification

The procedure started on 10/02/2025 14:49 GMT

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to accept change(s) to the agreed paediatric investigation plan and to the deferral.

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This decision is forwarded to the applicant, together with its annex and appendix.

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Final Decision Letter

MHRA-101767-PIP01-24-M01

Of 18/02/2025 08:55 GMT

On the adopted decision for TOFACITINIB CITRATE (MHRA-101767-PIP01-24-M01) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on modification of a paediatric investigation plan (including modification of a deferral included in that paediatric investigation plan)

This decision applies to a Modification for TOFACITINIB CITRATE, Film-coated tablet Prolonged-release film-coated tablet Age-appropriate oral liquid formulation Prolonged-release age-appropriate oral formulation , ORAL USE .

This decision is addressed to Pfizer Limited, Ramsgate Road, Sandwich, Kent, UNITED KINGDOM, CT139NJ

ANNEX I

1. Waiver

1.1 Condition:

Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis). The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 2 years of age. 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 Reason for granting waiver: 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(s):

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

2.2 Indication(s) targeted by the PIP:

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

2.3 Subset(s) of the paediatric population concerned by the paediatric development:

The paediatric population from 2 years of age to less than 18 years of age.

2.4 Pharmaceutical Form(s):

Film-coated tablet Prolonged-release film-coated tablet Age-appropriate oral liquid formulation Prolonged-release age-appropriate oral formulation

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	3	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	3	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	4	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, Modeling & Simulation Studies	3	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	0	Not applicable.
Other Measures	0	Not applicable.

3. Follow-up, completion and deferral of a PIP:

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	31/03/2027
Deferral of one or more studies contained in the paediatric investigation plan:	Yes