MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
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-100786-PIP01-22-M01

Scope of the Application

Active Substance(s)

TOFACITINIB CITRATE

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 the Decision

Pursuant to the Human Medicines Regulations 2012, Pfizer Limited submitted to the licensing authority on 24/11/2022 11:02 GMT an application for a Modification

The procedure started on 11/05/2023 10:16 BST

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-100786-PIP01-22-M01

Of 08/06/2023 07:01 BST

On the adopted decision for TOFACITINIB CITRATE (MHRA-100786-PIP01-22-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 waiver or deferral included in that paediatric investigation plan).

This decision applies to a Modification for TOFACITINIB CITRATE, Film-coated tablet, Oral solution , 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 ulcerative colitis. 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, Oral solution Route(s) of administration: ORAL USE Reason for granting waiver: on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of ulcerative colitis.

2.2 Indication(s) targeted by the PIP:

Treatment of children and adolescents from 2 years 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.

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

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

2.4 Pharmaceutical Form(s):

Film-coated tablet Oral solution

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of oral solution 1 mg/ml. Study 7 Deleted during procedure MHRA-100786-PIP01-22-M01. Study 8 Deleted during procedure MHRA-100786-PIP01-22-M01.
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 (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 years to less than 18 years of age with moderately to severely active ulcerative colitis.
Extrapolation, Modeling & Simulation Studies	2	Study 6 Modelling and simulation study to select doses for evaluating the use of tofacitinib in children from 2 years to less than 18 years of age with ulcerative colitis. Study 9 Deleted during procedure MHRA-100786-PIP01-22-M01. Study 10 Population PK analysis using data from the PK, efficacy

		and safety study in paediatric UC patients. Study 11 Deleted during procedure MHRA-100786-PIP01-22-M01.
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:	30/06/2026
Deferral of one or more studies contained in the paediatric investigation plan:	Yes