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

MHRA-100224-PIP01-21-M01

Scope of the Application

Active Substance(s)

etrasimod L-arginine

Condition(s)

Treatment of ulcerative colitis

Pharmaceutical Form(s)

Film-coated tablet. Age-appropriate oral solid dosage form.

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 21/06/2022 18:48 BST an application for a Modification

The procedure started on 06/12/2022 09:47 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-100224-PIP01-21-M01

Of 11/01/2023 21:42 GMT

On the adopted decision for etrasimod L-arginine (MHRA-100224-PIP01-21-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 etrasimod L-arginine, Film-coated tablet. Age-appropriate oral solid dosage form. , ORAL USE .

This decision is addressed to Pfizer Limited, Ramsgate Road, Sandwich, UNITED KINGDOM, CT13 9NJ

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 Age-appropriate oral solid dosage form Route(s) of administration: ORAL USE Reason for granting waiver: On the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of ulcerative colitis

2.2 Indication(s) targeted by the PIP:

Treatment of moderately or severely active ulcerative colitis

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 Age-appropriate oral solid dosage form

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of an age-appropriate oral solid dosage form.
Non-Clinical Studies	1	Study 2 (APD334.TOX.009) Definitive juvenile toxicity study in Sprague Dawley rats.
Clinical Studies	4	Study 3 (APD334-301) Randomised, double-blind, placebo-controlled study to assess efficacy and safety of etrasimod as compared to placebo in adolescents from 16 years to less than 18 years of age (and adults) with moderately to severely active ulcerative colitis (UC) over a 52-week treatment period. Study 4 (APD334-302) Randomised, double-blind, placebo-controlled study to assess efficacy after 12 weeks of treatment and safety of etrasimod as compared to placebo in adolescents from 16 years to less than 18 years of age (and adults) with moderately to severely active ulcerative colitis (UC). Study 5 (APD334-PED1, APD334-207) Open-label, single-arm, study to evaluate the efficacy, safety and pharmacokinetics of etrasimod, consisting of a 12-week induction period to evaluate the efficacy, safety and PK and pharmacodynamic (PD) relationship, and a 40-week treatment extension

		period to evaluate efficacy, PK, and long-term safety of etrasimod in adolescents from 12 years to less than 18 years of age with moderately to severely active ulcerative colitis (UC). Study 6 (APD334-PED2, APD334-208) Open-label, single-arm, study to evaluate the efficacy, safety and pharmacokinetics of etrasimod, consisting of a 12-week induction period to evaluate the efficacy, safety and PK and pharmacodynamic (PD) relationship, and a 40-week treatment extension period to evaluate efficacy, PK, and long-term safety of etrasimod in children from 2 years to less than 12 years of age with moderately to severely active ulcerative colitis (UC).
Extrapolation, Modeling & Simulation Studies	2	Study 7 (MODEL 1) Population pharmacokinetic model to predict PK exposures and determine appropriate doses in paediatric populations. Study 8 (MODEL 2) Population pharmacokinetic/pharmacodynamic model(s) (exposure-response analyses).
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:	No
Date of completion of the paediatric investigation plan:	30/09/2023
Deferral of one or more studies contained in the paediatric investigation plan:	Yes