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-100086-PIP01-21-M01

Scope of the Application

Active Substance(s)

UPADACITINIB

Condition(s)

Treatment of atopic dermatitis

Pharmaceutical Form(s)

Prolonged release tablet; Prolonged release capsule; Age appropriate oral solid dosage form; Age appropriate oral liquid dosage form

Route(s) of Administration

Oral use

Name / Corporate name of the PIP applicant

AbbVie Ltd

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, AbbVie Ltd submitted to the licensing authority on 07/04/2021 15:39 BST an application for a Modification

The procedure started on 25/11/2021 10:34 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-100086-PIP01-21-M01

Of 07/12/2021 09:12 GMT

On the adopted decision for UPADACITINIB (MHRA-100086-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 UPADACITINIB, Prolonged release tablet; Prolonged release capsule; Age appropriate oral solid dosage form; Age appropriate oral liquid dosage form , Oral use .

This decision is addressed to AbbVie Ltd, AbbVie House, Vanwall Road, Maidenhead, Berkshire, SL6 4UB, United Kingdom, Maidenhead, United Kingdom, SL6 4UB

ANNEX I

1. Waiver

1.1 Condition:

Treatment of atopic dermatitis The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 2 years of age Pharmaceutical form(s): Prolonged release tablet; Prolonged release capsule; Age appropriate oral solid dosage form; Age appropriate oral liquid dosage form 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 atopic dermatitis

2.2 Indication(s) targeted by the PIP:

Treatment of moderate to severe atopic dermatitis in children from 2 years of age who are candidates for systemic therapy

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

All subsets of the paediatric population from 2 years to less than 18 years of age

2.4 Pharmaceutical Form(s):

Prolonged release tablet; Prolonged release capsule; Age appropriate oral solid dosage form; Age appropriate oral liquid 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 (dispersible tablet or multi particulate granules) or age appropriate oral liquid dosage form.
Non-Clinical Studies	2	Study 2 Dose range-finding juvenile toxicity study. Study 3 Definitive juvenile toxicity study to evaluate toxicity and impact of upadacitinib on neonatal/ juvenile development.
Clinical Studies	6	Study 4 Open-label, multiple-dose study to evaluate the pharmacokinetics, safety, and tolerability (Part 1) and long term safety and tolerability (Part 2) of upadacitinib in children from 2 years to less than12 years with severe atopic dermatitis. Study 5 Double-blind, randomised, placebo-controlled study to evaluate the safety and efficacy of upadacitinib in adolescents (and adults) subjects with moderate to severe atopic dermatitis who are candidates for systemic therapy. Study 6 Double-blind, randomised, placebo-controlled study to evaluate safety and efficacy of upadacitinib in adolescents (and adults) with moderate to severe atopic dermatitis, who are candidates for systemic therapy in combination with topical corticosteroids. Study 7 Double-blind, randomised, placebo-

		controlled study to evaluate safety and efficacy of upadacitinib in adolescents (and adults) with moderate to severe atopic dermatitis, who are candidates for systemic therapy. Study 8 Double-blind, randomised, placebo-controlled, study to evaluate the safety and efficacy of upadacitinib as add on to standard of care in children form 2 years to less than 18 years with severe atopic dermatitis. Study 9 Open label extension study to evaluate the long-term safety and efficacy of upadacitinib monotherapy in children from 2 years to less than 18 years of age with severe atopic dermatitis.
Extrapolation, Modeling & Simulation Studies	2	Study 10 Pop PK to predict the initial paediatric dosages to be used in further clinical studies; PoP PK to confirm of modify the paediatric posology compared to the regimen used in clinical trials Study 11 Population exposure response model analyses to identify subgroups where this relationship is altered and may need posology changes or other risk mitigation measures.
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:	30/11/2024
Deferral of one or more studies contained in the paediatric investigation plan:	Yes