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 (MHRA-100093-PIP01-21-M03) and to the deferral

MHRA-100093-PIP01-21-M04

Scope of the Application

Active Substance(s)

UPADACITINIB

Condition(s)

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

Pharmaceutical Form(s)

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

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 01/02/2024 15:38 GMT an application for a Modification

The procedure started on 23/05/2024 17:56 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, and to link this PIP with related PIP Decisions covering all authorised indications of Upadacitinib for treatment of Crohn's disease, for treatment of vasculitides, for treatment of atopic dermatitis, for treatment of ulcerative colitis, for treatment of vitiligo and for treatment for systemic lupus erythematosus, including all subsequent modifications thereof.

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-100093-PIP01-21-M04

Of 04/07/2024 15:11 BST

On the adopted decision for UPADACITINIB (MHRA-100093-PIP01-21-M04) 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, Age-appropriate oral solid dosage form; Age-appropriate oral liquid dosage form; Prolonged-release tablet , ORAL USE .

This decision is addressed to AbbVie Ltd, AbbVie House, Vanwall Road, Maidenhead, UNITED KINGDOM, SL6 4UB

ANNEX I

1. Waiver

1.1 Condition:

Treatment of chronic idiopathic arthritis (including rheumatoid arthritis, psoriatic arthritis, spondyloarthritis and juvenile idiopathic arthritis). The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 1 year of age. Pharmaceutical form(s): Age-appropriate oral solid dosage form Age-appropriate oral liquid dosage form Prolonged-release tablet. 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, spondyloarthritis and juvenile idiopathic arthritis).

2.2 Indication(s) targeted by the PIP:

Treatment of Juvenile Idiopathic Arthritis.

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

The paediatric population from 1 year to less than 18 years of age.

2.4 Pharmaceutical Form(s):

Age-appropriate oral solid dosage form. Age-appropriate oral liquid dosage form Prolonged-release tablet.

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of 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	2	Study 4 Open-label, multiple dose study to evaluate the pharmacokinetics, safety, and tolerability and to confirm the dosing regimen of upadacitinib in children with active polyarticular course JIA. Study 5, deleted during procedure MHRA-100093-PIP01-21-M02. Study 6 Randomised, placebo-controlled, double-blind withdrawal study to evaluate the safety and efficacy of multiple doses of upadacitinib in children with active systemic JIA.
Extrapolation, Modeling & Simulation Studies	1	Study 7 Population pharmacokinetic two compartment model that characterises the pharmacokinetic parameters, the inter- and intra-

		subject variability, and relationship between pharmacokinetic parameters and the relevant covariates.
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:	31/08/2028
Deferral of one or more studies contained in the paediatric investigation plan:	Yes