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-100093-PIP01-21-M01

Scope of the Application

Active Substance(s)

UPADACITINIB

Condition(s)

Treatment of chronic idiopathic arthritis

Pharmaceutical Form(s)

Prolonged released tablet; Age-appropriate oral liquid dosage form; Age-appropriate oral solid 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 19/04/2021 22:25 BST an application for a Modification

The procedure started on 29/11/2021 17:07 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-100093-PIP01-21-M01

Of 07/12/2021 09:52 GMT

On the adopted decision for UPADACITINIB (MHRA-100093-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 released tablet; Age-appropriate oral liquid dosage form; Age-appropriate oral solid dosage form , Oral use .

This decision is addressed to AbbVie Ltd, Vanwall Business Park, 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 liquid dosage form; Age-appropriate oral solid 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 liquid dosage form; Age-appropriate oral solid 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	3	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 Randomised, placebo-controlled, double-blind withdrawal study to evaluate the safety and efficacy of upadacitinib in children with active polyarticular course JIA 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 characterizes 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