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-100308-PIP01-21-M01

Scope of the Application

Active Substance(s)

AZILSARTAN MEDOXOMIL

Condition(s)

Treatment of hypertension

Pharmaceutical Form(s)

Granules for oral suspension, Tablet

Route(s) of Administration

Oral use

Name / Corporate name of the PIP applicant

Takeda UK Ltd

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Takeda UK Ltd submitted to the licensing authority on 12/10/2021 12:16 BST an application for a Modification

The procedure started on 28/04/2022 11:40 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-100308-PIP01-21-M01

Of 10/05/2022 16:43 BST

On the adopted decision for AZILSARTAN MEDOXOMIL (MHRA-100308-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 AZILSARTAN MEDOXOMIL, Granules for oral suspension, Tablet , Oral use .

This decision is addressed to Takeda UK Ltd, 1 Kingdom Street, London, United Kingdom, W2 6BD

ANNEX I

1. Waiver

1.1 Condition:

1.1 Condition: Treatment of hypertension The waiver applies / applied to: Paediatric Subset(s): Preterm newborn infants; Term newborn infants (from birth to less than 28 days); Infants and children (from 28 days to less than 24 months) Pharmaceutical form(s): Granules for oral suspension; Tablet 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 hypertension

2.2 Indication(s) targeted by the PIP:

Treatment of Essential (primary) hypertension; Treatment of Secondary hypertension

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):

Granules for oral suspension; Tablet

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of age appropriate formulation (granules for oral suspension).
Non-Clinical Studies	4	Study 2 Repeat-dose range-finding toxicity study in neonatal rats. Study 3 Repeat-dose toxicity study with recovery in neonatal rats. Study 4 A detailed comparative analysis of the toxicity profile of azilsartan compared to candesartan. Study 5 Repeat dose toxicity with recovery in juvenile rats.
Clinical Studies	4	Study 6 Relative bioavailability, safety, and tolerability study in adults. Study 7 Single-dose PK, safety, and tolerability of TAK 491 in children and adolescents. Study 8 Randomised, double-blind, active-controlled, 6-week dose-ranging safety and efficacy study with a 2-week, randomised, double-blind, placebo-controlled withdrawal phase and 44-week open-label extension in children aged 6 years to less than 18 years with essential and secondary hypertension. Study 9 Randomised, double-blind, 6-week dose-ranging safety and efficacy study with a 2-week randomized double-blind, placebo-controlled withdrawal phase and 2-year open-label extension in young children 2 years and older and with a weight of less than 25 kg with mild to moderate secondary hypertension.

Extrapolation, Modeling & Simulation Studies	0	Not applicable
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:	31/01/2022
Deferral of one or more studies contained in the paediatric investigation plan:	Yes