MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

gov.uk/mhra

Decision Cover Letter

Decision of the licensing authority to:

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

MHRA-101336-PIP01-24-M01

Scope of the Application

Active Substance(s)

DENGUE VIRUS SEROTYPE 2 EXPRESSING DENGUE VIRUS SEROTYPE 1 SURFACE PROTEINS LIVE ATTENUATED; DENGUE VIRUS SEROTYPE 2 EXPRESSING DENGUE VIRUS SEROTYPE 3 SURFACE PROTEINS LIVE ATTENUATED; DENGUE VIRUS SEROTYPE 2 EXPRESSING DENGUE VIRUS SEROTYPE 4 SURFACE PROTEINS LIVE ATTENUATED; DENGUE VIRUS SEROTYPE 2 LIVE ATTENUATED

Condition(s)

Prevention of dengue fever

Pharmaceutical Form(s)

Powder and solvent for solution for injection

Route(s) of Administration

SUBCUTANEOUS USE

Name / Corporate name of the PIP applicant

Takeda Vaccines, Inc.

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Takeda Vaccines, Inc. submitted to the licensing authority on 18/01/2024 11:35 GMT an application for a Modification

The procedure started on 22/04/2024 11:02 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.

MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

gov.uk/mhra

Final Decision Letter

MHRA-101336-PIP01-24-M01

Of 25/04/2024 10:21 BST

On the adopted decision for DENGUE VIRUS SEROTYPE 2 EXPRESSING DENGUE VIRUS SEROTYPE 1 SURFACE PROTEINS LIVE ATTENUATED; DENGUE VIRUS SEROTYPE 2 EXPRESSING DENGUE VIRUS SEROTYPE 3 SURFACE PROTEINS LIVE ATTENUATED; DENGUE VIRUS SEROTYPE 2 EXPRESSING DENGUE VIRUS SEROTYPE 4 SURFACE PROTEINS LIVE ATTENUATED; DENGUE VIRUS SEROTYPE 2 LIVE ATTENUATED (MHRA-101336-PIP01-24-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 DENGUE VIRUS SEROTYPE 2 EXPRESSING DENGUE VIRUS SEROTYPE 1 SURFACE PROTEINS LIVE ATTENUATED; DENGUE VIRUS SEROTYPE 2 EXPRESSING DENGUE VIRUS SEROTYPE 3 SURFACE PROTEINS LIVE ATTENUATED; DENGUE VIRUS SEROTYPE 2 EXPRESSING DENGUE VIRUS SEROTYPE 4 SURFACE PROTEINS LIVE ATTENUATED; DENGUE VIRUS SEROTYPE 2 LIVE ATTENUATED, Powder and solvent for solution for injection , SUBCUTANEOUS USE .

This decision is addressed to Takeda Vaccines, Inc., 40 Lansdowne Street, Cambridge, MA, UNITED STATES OF AMERICA, 02139

ANNEX I

1. Waiver

1.1 Condition:

Prevention of dengue fever. The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 2 months of age. Pharmaceutical form(s): Powder and solvent for solution for injection Route(s) of administration: SUBCUTANEOUS USE Reason for granting waiver: On the grounds the specific medicinal product is likely to be ineffective.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Prevention of dengue fever.

2.2 Indication(s) targeted by the PIP:

Active immunisation against dengue fever caused by dengue virus serotypes 1, 2, 3 and 4.

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

The paediatric population from 2 months to less than 18 years of age.

2.4 Pharmaceutical Form(s):

Powder and solvent for solution for injection

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable.
Non-Clinical Studies	0	Not applicable.
Clinical Studies	7	Study 1 (DEN-204) Randomised, double-blind, placebo-controlled trial to evaluate safety and immunogenicity of different schedules of Tetravalent Dengue Vaccine (TDV) in subjects 2 years to less than 18 years of age. Study 2 (DEN-301, Parts 1 and 2) Randomised, double-blind, placebo-controlled study to evaluate efficacy, safety and immunogenicity of TDV in children and adolescents 4 years to 16 years of age. Study 3 (DEN-301, Part 3) Randomised, double-blind, placebo-controlled study to evaluate the long-term safety, immunogenicity and efficacy of TDV in children and adolescents 4 years to 16 years of age. Study 4 (DEN-315) Randomised, double-blind, placebo-controlled trial to investigate safety and immunogenicity of 2 doses of TDV in male and female adolescents aged 12 years to 17 years. Study 5

		(DEN-306) Randomised, double blind trial to evaluate the safety and immunogenicity of 2 doses of TDV administered within the routine vaccine schedule of infants and toddlers 6 months to less than 21 months of age. Study 6 (DEN-316) Randomised, double blind trial to evaluate safety and immunogenicity of TDV co-administered with Measles, Mumps, and Rubella Virus Vaccine Live (MMR) infants and toddlers 12 months to less than 13 months of age. Study 7 (DEN-317) This study was deleted during procedure MHRA-101336-PIP01-24-M01. Study 8 (DEN-318) This study was deleted during procedure MHRA-101336-PIP01-24-M01. Study 9 (DEN-319) Randomised, open label trial to evaluate safety and immunogenicity of TDV co-administered with routine infant vaccines, according to different immunization schedules in infants 2 months to less than 6 months of age. Study 10 (DEN-320) This study was deleted during procedure MHRA-101336-PIP01-24-M01.
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:	31/07/2032
Deferral of one or more studies contained in the paediatric investigation plan:	Yes