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

gov.uk/mhra

Decision Cover Letter

Decision of the licensing authority to:

agree a paediatric investigation plan and grant a deferral and grant a waiver

MHRA-100096-PIP01-21

Scope of the Application

Active Substance(s)

Live, attenuated, dengue virus, serotype 1 (DENV1) ; Live, attenuated, chimeric dengue virus, serotype 2 (DENV2) ; Live, attenuated, dengue virus, serotype 3 (DENV3) ; Live, attenuated, dengue virus, serotype 4 (DENV4)

Condition(s)

Prevention of dengue disease

Pharmaceutical Form(s)

Powder and solvent for solution for injection

Route(s) of Administration

SUBCUTANEOUS USE

Name / Corporate name of the PIP applicant

Merck Sharp & Dohme (UK) Ltd

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Merck Sharp & Dohme (UK) Ltd submitted to the licensing authority on 28/05/2021 12:38 BST an application for a Paediatric Investigation Plan

The procedure started on 01/03/2022 18:15 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 agree a paediatric investigation plan and grant a deferral and grant a waiver

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-100096-PIP01-21

Of 15/08/2023 07:50 BST

On the adopted decision for Live, attenuated, dengue virus, serotype 1 (DENV1) ; Live, attenuated, chimeric dengue virus, serotype 2 (DENV2) ; Live, attenuated, dengue virus, serotype 3 (DENV3) ; Live, attenuated, dengue virus, serotype 4 (DENV4) (MHRA-100096-PIP01-21) 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 a paediatric investigation plan

This decision applies to a Paediatric Investigation Plan for Live, attenuated, dengue virus, serotype 1 (DENV1) ; Live, attenuated, chimeric dengue virus, serotype 2 (DENV2) ; Live, attenuated, dengue virus, serotype 3 (DENV3) ; Live, attenuated, dengue virus, serotype 4 (DENV4), Powder and solvent for solution for injection , Subcutaneous use .

This decision is addressed to Merck Sharp & Dohme (UK) Ltd, 120 Moorgate , London, United Kingdom, EC2M 6UR

ANNEX I

1. Waiver

1.1 Condition:

Prevention of dengue disease 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 that the specific medicinal product is likely to be ineffective

2. Paediatric Investigation Plan:

2.1 Condition(s):

Prevention of dengue disease

2.2 Indication(s) targeted by the PIP:

Prevention of dengue disease

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	3	Study 1 (DEN-03-IB) Randomised, multicentre, double-blind, placebo-controlled study to evaluate the efficacy and safety of a single dose of the Dengue 1,2,3,4 (live attenuated) vaccine produced by the Butantan Institute (Butantan-DV Dengue vaccine) in children from 2 years to less than 18 years of age for the prevention of dengue disease. Study 2 (CLI-PED 2-17YO) Randomised, double-blind, placebo-controlled safety and immunogenicity study of a single dose of live, attenuated, dengue virus, serotype 1 (DENV1), live, attenuated, chimeric dengue virus, serotype 2 (DENV2), live, attenuated, dengue virus, serotype 3 (DENV3), live, attenuated, dengue virus, serotype 4 (DENV4) (V181) in children from 2 years to less than 18 years of age for the prevention of dengue disease. Study 3 (CLI-PED 2-23MO) Randomised, double-blind, placebo-controlled safety and immunogenicity study of a

		single dose of live, attenuated, dengue virus, serotype 1 (DENV1), live, attenuated, chimeric dengue virus, serotype 2 (DENV2), live, attenuated, dengue virus, serotype 3 (DENV3), live, attenuated, dengue virus, serotype 4 (DENV4) (V181) in children from 2 months of age to 23 months of age in endemic countries, for the prevention of dengue disease.
Extrapolation, Modeling & Simulation Studies	0	Not applicable.
Other Studies	2	Study 4 (CLI Concom MMR Pent) Randomised, double-blind, placebo controlled, cross-over safety and immunogenicity study in endemic countries of a single dose of live, attenuated, dengue virus, serotype 1 (DENV1), live, attenuated, chimeric dengue virus, serotype 2 (DENV2), live, attenuated, dengue virus, serotype 3 (DENV3), live, attenuated, dengue virus, serotype 4 (DENV4) (V181) in children from 12 months of age to 15 months of age at enrolment, for the prevention of dengue disease. Study 5 (CLI Concom YF) Open label safety and immunogenicity study in endemic countries of a single dose of live, attenuated, dengue virus, serotype 1 (DENV1), live, attenuated, chimeric dengue virus, serotype 2 (DENV2), live, attenuated, dengue virus, serotype 3 (DENV3), live, attenuated, dengue virus, serotype 4 (DENV4) (V181) in children from 12 months of age to 18 months of age at enrolment, for the prevention of dengue disease.
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:	No
Date of completion of the paediatric investigation plan:	28/02/2030
Deferral of one or more studies contained in the paediatric investigation plan:	Yes