EMA/915714/2022

European Medicines Agency decision

P/0521/2022

of 30 December 2022

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver 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) (EMEA-002999-PIP01-21) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Disclaimer

This decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

Only the English text is authentic.

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The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the application submitted by Merck Sharp & Dohme (Europe), Inc. on 22 March 2021 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 11 November 2022, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation and Article 13 of said Regulation,

Having regard to Article 25 of Regulation (EC) No 1901/2006,

Whereas:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a deferral.

(4) It is therefore appropriate to adopt a decision granting a waiver.

[1] OJ L 378, 27.12.2006, p.1, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

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, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A deferral 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, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

A waiver 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, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 4

This decision is addressed to Merck Sharp & Dohme (Europe), Inc., 5 Clos du Lynx, 1200 - Brussels Belgium.

EMA/PDCO/686523/2022 corr[1]
Amsterdam, 11 November 2022

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and a waiver

EMEA-002999-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)

Invented name and authorisation status:

See Annex II

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 (Europe), Inc.

[1] 13 December 2022

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Merck Sharp & Dohme (Europe), Inc. submitted for agreement to the European Medicines Agency on 22 March 2021 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 27 April 2021.

Supplementary information was provided by the applicant on 8 August 2022.

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 17(1) of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation;
   - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(a) of said Regulation, on the grounds that the specific medicinal product is likely to be ineffective or unsafe in part or all of the paediatric population.

   The Paediatric Committee member of Norway agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the agreed paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annexes and appendix.

Annex I

The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed paediatric investigation plan (PIP)

1. Waiver

1.1. Condition:

Prevention of dengue disease

The waiver applies to:

- the paediatric population from birth to less than 2 months of age;
- powder and solvent for solution for injection; subcutaneous use;
- on the grounds that the specific medicinal product is likely to be ineffective.

2. Paediatric investigation plan

2.1. Condition:

Prevention of dengue disease

2.1.1. Indication(s) targeted by the PIP

Prevention of dengue disease

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From 2 months of age to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Powder and solvent for solution for injection

2.1.4. Measures

Area	Description
Quality-related studies	Not applicable
Non-clinical studies	Not applicable
Clinical studies	**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. **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.
Modelling and simulation studies	Not applicable
Other studies	Not applicable
Extrapolation plan	Not applicable

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By July 2028
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

The product is not authorised anywhere in the European Community.