Dengvaxia

Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion/ Notification [1] issued on	Commission Decision Issued [2] / amended on	Product Information affected [3]	Summary
T/0033	Transfer of Marketing Authorisation	27/11/2024	12/12/2024	SmPC, Labelling and PL	
II/0032	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	28/11/2024	n/a		

[1] Notifications are issued for type I variations and Article 61(3) notifications (unless part of a group including a type II variation or extension application or a worksharing application). Opinions are issued for all other procedures.
[2] A Commission decision (CD) is issued for procedures that affect the terms of the marketing authorisation (e.g. summary of product characteristics, annex II, labelling, package leaflet). The CD is issued within two months of the opinion for variations falling under the scope of Article 23.1a(a) of Regulation (EU) No. 712/2012, or within one year for other procedures.
[3] SmPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet).

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II/0031	Submission of final study report of DNG15, listed in the RMP as category 3. DNG15 was a prospective, multinational, non-interventional, observational study aiming to assess the risk of AEs associated with CYD dengue vaccine in the real-world immunization setting. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	05/09/2024	n/a		Not applicable.
II/0030	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	18/07/2024	n/a		
II/0029	Submission of the final report from study CYD69 listed as a category 3 study in the RMP. This is an Observational study: Effectiveness of the tetravalent dengue vaccine, CYD-TDV (DENGVAXIA) in the Philippines. This procedure fulfils post-authorisation commitment MEA 005 for Dengvaxia. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	27/06/2024	n/a		
N/0028	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	20/12/2023	12/12/2024	PL	

R/0027	Renewal of the marketing authorisation.	22/06/2023	11/08/2023	SmPC and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Dengvaxia in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
PSUSA/10740 /202212	Periodic Safety Update EU Single assessment - dengue tetravalent vaccine (live, attenuated) [Chimeric yellow fever dengue virus serotype 1 (live, attenuated) / Chimeric yellow fever dengue virus serotype 2 (live, attenuated) / Chimeric yellow fever dengue virus serotype 3 (live, attenuated) / Chimeric yellow fever dengue virus serotype 4 (live, attenuated)]	06/07/2023	n/a		PRAC Recommendation - maintenance
IB/0026	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	24/03/2023	n/a		
IG/1559	B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking	24/10/2022	n/a		
IB/0023	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	13/07/2022	n/a		
PSUSA/10740 /202112	Periodic Safety Update EU Single assessment - dengue tetravalent vaccine (live, attenuated) [Chimeric yellow fever dengue virus serotype 1 (live, attenuated) / Chimeric yellow fever dengue virus	07/07/2022	n/a		PRAC Recommendation - maintenance

	serotype 2 (live, attenuated) / Chimeric yellow fever dengue virus serotype 3 (live, attenuated) / Chimeric yellow fever dengue virus serotype 4 (live, attenuated)]				
IB/0022	B.II.c.1.z - Change in the specification parameters and/or limits of an excipient - Other variation	21/06/2022	n/a		
PSUSA/10740 /202106	Periodic Safety Update EU Single assessment - dengue tetravalent vaccine (live, attenuated) [Chimeric yellow fever dengue virus serotype 1 (live, attenuated) / Chimeric yellow fever dengue virus serotype 2 (live, attenuated) / Chimeric yellow fever dengue virus serotype 3 (live, attenuated) / Chimeric yellow fever dengue virus serotype 4 (live, attenuated)]	13/01/2022	n/a		PRAC Recommendation - maintenance
II/0013	Update of sections 4.2 and 5.1 of the SmPC based on final results from study CYD65, listed as a category 3 study in the RMP; this is a Phase II, observer-blind, placebo-controlled trial in order to assess Immunogenicity and Safety of Tetravalent Dengue Vaccine Given in 1-, 2-, or 3-Dose Schedules Followed by a Single Booster. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	11/11/2021	09/12/2021	SmPC and PL	Results of study CYD65 showed no or modest transient increase of neutralizing Ab titers after the booster in dengue immune subjects. Why there is a lack of/limited booster effect with Dengvaxia remains not understood in terms of mechanisms and clinical implications. In the absence of immune correlates of protection, whether the absence or modest increases in Ab titers, plasmablasts, and memory B cells, do not translate or could translate in protection against dengue disease, during the first year post-boost or during a longer period, is not known. It was thus considered that the added value and timing for booster dose(s) have not been established. This paragraph was added to the Posology Section of the SmPC:

					"The added value of and appropriate timing for booster dose(s) have not been established. Current available data are included in section 5.1." Cross-referred to the following text in Section 5.1: "The effect of a booster dose was assessed in subjects 9-50 years living in endemic areas after a 3-dose schedule (studies CYD63, CYD64, CYD65). No or modest transient increase of neutralizing Ab titers was observed after the boost. The booster effect was variable across serotypes and studies. Why there is a lack/limited booster effect with Dengvaxia remains not understood in terms of mechanisms and clinical implications." For more information, please refer to the Summary of Product Characteristics.
II/0012	Extension of indication to include paediatric population from 6 years of age for Dengvaxia; as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC and sections 1, 2 and 4 of the Package Leaflet are updated. Furthermore, the MAH takes the opportunity to add an instruction for the installation of the needle in the SmPC and the Package Leaflet of the single-dose presentation. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	11/11/2021	09/12/2021	SmPC and PL	Please refer to Scientific Discussion 'Dengvaxia -H-C-004171-II-0012'.
II/0011	Update of the PI impacting the Therapeutic	11/11/2021	09/12/2021	SmPC and PL	Please refer to Scientific Discussion 'Dengvaxia -H-C-

	Indications section to further detail the conditions for the eligibility to pre-vaccination serostatus screening. As a consequence, sections 4.1, 4.2, 4.4 and 5.1 of the SmPC and sections 1, 2 and 3 of the Package Leaflet are updated accordingly. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				004171-II-0011'.
II/0016/G	This was an application for a group of variations. Update of section 4.5. of the SmPC to include coadministration data on human papillomavirus (HPV) vaccines and tetanus, diphtheria, and pertussis (Tdap) vaccine from CYD67, CYD71 and CYD66 final study reports respectively (final reports from three MEA studies listed as category 3 studies in the RMP); these studies are focused on immunogenicity and safety of the concomitant administration. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. The RMP version 6.3 is approved with this variation C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	02/12/2021	28/11/2022	SmPC and PL	Given that the population of indication of Dengvaxia includes preadolescents and adolescents, the MAH conducted three co-administration studies with vaccines used in this age range: human papillomavirus (HPV) vaccines (studies CYD67 and CYD71, respectively) and tetanus, diphtheria, and pertussis (Tdap) vaccine in study CYD66. These studies assessed the immunogenicity and safety following the concomitant administration, compared to sequential administration, of Dengvaxia with the other vaccines. The final clinical study reports for these co-administration Phase III studies were submitted. The results support allowing concomitant administration of Dengvaxia with bivalent HPV, quadrivalent HPV, and Tdap vaccines. Section 4.5 of the Dengvaxia SmPC was updated to reflect the statistical limitation regarding the unmet non-inferiority criteria for the HPV vaccines and Dengvaxia in CYD67 and CYD71 studies. The results of these two studies are appropriately described in the SmPC, as well as those of

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				study CYD66. For more information, please refer to the Summary of Product Characteristics.
IB/0020	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	12/11/2021	n/a		
PSUSA/10740 /202012	Periodic Safety Update EU Single assessment - dengue tetravalent vaccine (live, attenuated) [Chimeric yellow fever dengue virus serotype 1 (live, attenuated) / Chimeric yellow fever dengue virus serotype 2 (live, attenuated) / Chimeric yellow fever dengue virus serotype 3 (live, attenuated) / Chimeric yellow fever dengue virus serotype 4 (live, attenuated)]	08/07/2021	n/a		PRAC Recommendation - maintenance
II/0018	Submission of the final report from study DNG10042, listed as a category 3 study in the RMP. This report summarises the findings on the dengue vaccine (Dengvaxia) effectiveness against virologically confirmed symptomatic infection, carried out after the mass vaccination program conducted by the Brazilian state of Paraná from 2016 to 2018. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	10/06/2021	n/a		
PSUSA/10740 /202006	Periodic Safety Update EU Single assessment - dengue tetravalent vaccine (live, attenuated)	14/01/2021	n/a		PRAC Recommendation - maintenance

	[Chimeric yellow fever dengue virus serotype 1 (live, attenuated) / Chimeric yellow fever dengue virus serotype 2 (live, attenuated) / Chimeric yellow fever dengue virus serotype 3 (live, attenuated) / Chimeric yellow fever dengue virus serotype 4 (live, attenuated)]				
IB/0015	B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data	20/11/2020	n/a		
PSUSA/10740 /201912	Periodic Safety Update EU Single assessment - dengue tetravalent vaccine (live, attenuated) [Chimeric yellow fever dengue virus serotype 1 (live, attenuated) / Chimeric yellow fever dengue virus serotype 2 (live, attenuated) / Chimeric yellow fever dengue virus serotype 3 (live, attenuated) / Chimeric yellow fever dengue virus serotype 4 (live, attenuated)]	09/07/2020	n/a		PRAC Recommendation - maintenance
IB/0009/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits B.II.d.1.z - Change in the specification parameters	23/04/2020	17/09/2020	SmPC, Labelling and PL	

	and/or limits of the finished product - Other variation B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation B.II.e.6.b - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that does not affect the product information B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State				
II/0007/G	This was an application for a group of variations. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	13/02/2020	n/a		
IB/0006/G	This was an application for a group of variations. B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data B.I.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change to an approved stability protocol	13/02/2020	n/a		

PSUSA/10740 /201906	Periodic Safety Update EU Single assessment - dengue tetravalent vaccine (live, attenuated) [Chimeric yellow fever dengue virus serotype 1 (live, attenuated) / Chimeric yellow fever dengue virus serotype 2 (live, attenuated) / Chimeric yellow fever dengue virus serotype 3 (live, attenuated) / Chimeric yellow fever dengue virus serotype 4 (live, attenuated)]	16/01/2020	n/a		PRAC Recommendation - maintenance
II/0003/G	This was an application for a group of variations. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	19/09/2019	17/09/2020	SmPC, Annex II, Labelling and PL	
IA/0004/G	This was an application for a group of variations. B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph	16/05/2019	n/a		

	of the Ph. Eur. or national pharmacopoeia of a Member State				
IB/0002	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	22/02/2019	n/a		