MenQuadfi

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
II/0027	Submission of the final report from study MET52, listed as a category 3 study in the RMP. This was a Phase III, open-label, randomised, parallel-group, active-controlled, multi-centre study to evaluate the immunogenicity and describe the safety of MenACYW conjugate vaccine when administered concomitantly	11/04/2024	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).

	with a Meningococcal Group B vaccine and other routine paediatric vaccines as part of the National Immunisation Schedule in healthy infants and toddlers in the United Kingdom. The RMP version 2.0 has also been submitted. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				
WS/2635	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.b.z - Change in control of the AS - Other variation	21/03/2024	n/a		
IA/0033	A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release)	21/02/2024	n/a		
PSUSA/10044 /202304	Periodic Safety Update EU Single assessment - meningococcal group a, c, w135, y conjugate vaccine (conjugated to tetanus toxoid carrier protein)	30/11/2023	n/a		PRAC Recommendation - maintenance
IB/0028/G	This was an application for a group of variations. B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	22/11/2023		SmPC and PL	

	B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Biological/immunological medicinal product in accordance with an approved stability protocol				
WS/2525/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological substance which may have a significant impact on the medicinal product and is not related to a protocol B.I.a.1.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The change relates to a biological AS or a starting material [-] used in the manufacture of a biological/immunological product B.I.b.z - Change in control of the AS - Other variation B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer	16/11/2023	n/a		
WS/2495	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.	13/07/2023	n/a		

	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation				
WS/2469	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	15/06/2023	n/a		
IB/0022/G	This was an application for a group of variations. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	26/05/2023	n/a		
N/0021	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	27/02/2023	31/03/2023	Labelling and PL	
IB/0020	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	10/01/2023	n/a		
II/0018/G	This was an application for a group of variations.	15/12/2022	31/03/2023	SmPC, Annex	The key SmPC text resulting from this variation read as

	Update of sections 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC in order to add long term antibody persistence at least 3 years after primary vaccination, immunogenicity and safety of a booster dose of MenQuadfi in adolescents, adults, and older adults, as well as co-administration data with meningococcal serogroup B vaccine in adolescents and adults, in order to fulfil ANX/002 and ANX/003 based on final results from studies MET59 and MEQ00066, respectively, listed as Annex-II obligations. MET59 is a phase 3b, open-label, partially randomized, parallel-group, active-controlled, multi-center study evaluating the immunogenicity and safety of a booster dose of an investigational quadrivalent MenACYW conjugate vaccine in adolescents and adults, while MEQ00066 is a phase 3, two-stage, randomized, open-label, multi-center trial evaluating the safety and immunogenicity of a single dose of MenACYW conjugate vaccine at least 3 years following initial vaccination with either Menomune vaccine or MenACYW conjugate vaccine in older adults. The Annex II and Package Leaflet are updated accordingly. The RMP version 1.2 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI. 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			II and PL	follows: - Section 4.2. Posology Long-term antibody persistence data following vaccination with MenQuadfi are available up to 7 years after vaccination (see sections 4.4 and 5.1). - Section 4.4. Protection Waning of serum bactericidal antibody titres against serogroup A when using human complement in the assay (hSBA) has been reported for MenQuadfi […]. However, if an individual is expected to be at particular risk of exposure to serogroup A and received a dose of MenQuadfi more than approximately one year previously, consideration may be given to administering a booster dose. - Section 4.5: Use with other vaccines There was no impact on the immune response to MenQuadfi when a meningococcal serogroup B vaccine was co-administered. - Section 4.8. Summary of the safety profile In one additional clinical study, adolescents and adults 13-26 years of age primed with MenQuadfi 3-6 years previously received MenQuadfi co-administered with meningococcal serogroup B (MenB) vaccine, Trumenba (N=93) or Bexsero (N=92). Rates and intensity of systemic reactions within 7 days following vaccination tended to be higher when MenQuadfi was given concomitantly with MenB vaccine than when MenQuadfi was given alone. The most common solicited

	new quality, preclinical, clinical or pharmacovigilance data				systemic reaction was myalgia, of mild intensity, which was experienced more frequently in adolescents and adults who received MenQuadfi and MenB vaccine concomitantly (Trumenba, 65.2%; Bexsero, 63%) compared to those who received MenQuadfi alone (32.8%). - Section 5.1. Immunogenicity Antibody persistence after primary vaccination and immunogenicity of a booster dose was assessed in three studies in children (4-5 years of age), adolescents and adults (13-26 years of age), and older adults (≥59 years of age). Clinical data on the persistence of antibody response ≥3 years after primary vaccination with MenQuadfi in children (4-5 years of age), adolescents and adults (13-26 years of age), and older adults (≥ 59 years of age) are available. Clinical data on booster vaccination with MenQuadfi in those subjects are also available.
PSUSA/10044 /202204	Periodic Safety Update EU Single assessment - meningococcal group a, c, w135, y conjugate vaccine (conjugated to tetanus toxoid carrier protein)	01/12/2022	n/a		PRAC Recommendation - maintenance
IB/0017	B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place	24/05/2022	n/a		
II/0016/G	This was an application for a group of variations. B.II.f.1.c - Stability of FP - Change in storage	22/04/2022	31/03/2023	SmPC, Labelling and	

	conditions for biological medicinal products, when the stability studies have not been performed in accordance with an approved stability protocol B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes			PL	
N/0015	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	02/03/2022	04/04/2022	Labelling	
II/0013	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	17/02/2022	04/04/2022	SmPC	
IG/1465	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	14/12/2021	n/a		
IB/0012/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site 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	07/12/2021	04/04/2022	SmPC, Labelling and PL	

IB/0010	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	15/11/2021	n/a		
WS/2101	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	02/09/2021	n/a		
II/0006	Update of section 5.1 of the SmPC based on final results from study MET62, listed in the Annex II (category 1 in the RMP); this is a study to investigate immunogenicity and safety of an investigational quadrivalent meningococcal conjugate vaccine administered as a booster dose in children vaccinated 3 years earlier as toddlers (ANX 001). In addition, the MAH took the opportunity to include minor editorial changes in Annex II of the product information. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	02/09/2021	04/04/2022	SmPC and Annex II	Please refer to Scientific Discussion 'MenQuadfi-H-C-005084-II-0006'
IAIN/0009/G	This was an application for a group of variations. B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP -	26/07/2021	04/04/2022	Annex II and PL	

	Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site				
II/0001/G	This was an application for a group of variations. B.II.d.z - Change in control of the Finished Product - Other variation B.II.b.2.c.3 - Change to importer, batch release arrangements and quality control testing of the FP - Including batch control/testing for a biol/immunol product and any of the test methods is a biol/immunol/immunochemical method	20/05/2021	n/a		
IB/0005/G	This was an application for a group of variations. B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate	12/05/2021	n/a		
WS/2034	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.	15/04/2021	n/a		

	B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate				
IA/0004	A.7 - Administrative change - Deletion of manufacturing sites	05/03/2021	04/04/2022	SmPC, Annex II and PL	
IAIN/0003/G	This was an application for a group of variations. B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.II.d.1.c - Change in the specification parameters and/or limits of the finished product - Addition of a new specification parameter to the specification with its corresponding test method B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits B.I.a.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging	26/02/2021	n/a		

	site				