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/0037	Update of section 4.8 of the SmPC in order to add "Febrile convulsions" and "seizures" to the list of adverse drug reactions (ADRs) with frequency not known, based on a safety review. The Package Leaflet is updated accordingly. The MAH took the opportunity to include editorial changes in the	23/01/2025		SmPC and PL	

[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).

	product information. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IB/0040	B.I.b.z - Change in control of the AS - Other variation	19/12/2024	n/a		
T/0039	Transfer of Marketing Authorisation	16/10/2024	13/11/2024	SmPC, Labelling and PL	
II/0034/G	This was an application for a group of variations. Grouped application comprising two type II variations as follows: C.I.4 - Update of section 5.1 of the SmPC in order to add 5 years persistence of immune response based on final results from study MEQ00066. MEQ00066 was a Phase III, two-stage, randomised, open-label, multi-centre trial to evaluate the immunogenicity and safety of a single dose of MenACYW conjugate vaccine at least 3 years after a prior dose of either MenACYW conjugate vaccine or Menomune. C.I.4 – Update of section 5.1 of the SmPC in order to add immune persistence and booster response data in children based on interim results from study MEQ00073. MEQ00073 is a Phase IIIb, open-label, multi-centre study to evaluate the immunogenicity and safety of a booster dose of MenQuadfi administered to children and describe 5- and/or 10-	24/10/2024		SmPC and Annex II	SmPC new text Section 5.1 Immunogenicity MenQuadfi when used as a booster vaccination was assessed in one pivotal study (subjects 15-55 years of age) and in four additional studies: two in children 3 years and 5 years after primary vaccination as toddlers 12 through 23 months of age, one in adolescents and adults 3-6 years after primary vaccination, and one in older adults 3, 5 and 6-7 years after primary vaccination at ≥ 56 years of age. In addition, clinical data on the persistence of antibody response from at least 3 years and up to 7 years after primary vaccination with MenQuadfi are available in these additional studies. […] Persistence of immune response and MenQuadfi booster response Antibody persistence following primary vaccination in toddlers, adolescents and young adults, and older adults was assessed from at least 3 years and up to 7 years after

	year immune persistence of MenQuadfi after primary vaccination. Annex II is also being updated. In addition, the MAH took the opportunity to introduce 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 new quality, preclinical, clinical or pharmacovigilance data				primary vaccination. The immunogenicity of a MenQuadfi booster dose was also assessed. […] Persistence of immune response and MenQuadfi booster response in children 6 through 7 years of age MEQ00073 (NCT04936685) evaluated the antibody persistence of a primary dose, immunogenicity and safety of a booster dose of MenQuadfi in children 6 through 7 years of age who had previously received a primary dose of MenQuadfi 5 years earlier as part of study MET51 when they were 12 through 23 months of age. For all serogroups, the 5Y post-primary (pre-booster) GMTs were higher than the pre-primary GMTs, indicative of persistence of immune response. After the booster dose, seroprotection rates were nearly 100% for all serogroups in children primed with MenQuadfi (98.9%, 97.7%, 100%, and 100% for serogroups A, C, W, and Y, respectively). […] Response in subjects according to MenC vaccination status before priming with MenQuadfi in MET51 The antibody responses against serogroup C following administration of a booster dose of MenQuadfi were comparable regardless of MenC vaccination status during their first year of life before priming with MenQuadfi 5 years earlier in MET51. […] Persistence of immune response and MenQuadfi booster response in adults 59 years of age and older 5 years persistence A subset of subjects (N=52) who were assessed for antibody persistence at 3 years and did not receive the booster dose were re-assessed for antibody persistence at 5 years at which time they received a booster dose of MenQuadfi. In MenQuadfi-primed subjects, hSBA GMTs for

					serogroups C, W and Y 5Y post-primary dose trended higher than the pre-priming GMTs (and were comparable for serogroup A). Following the MenQuadfi booster dose, seroprotection rates were 100% for serogroups A, C, and Y, and 95.0% for serogroup W in subjects primed with MenQuadfi and 87.5%, 62.5%, 87.% and 68.8% for serogroups A, C, W and Y, respectively, for those primed with MenACWY-PS. Additionally, hSBA GMTs were higher and seroresponse rates were higher or trended higher for all serogroups in subjects primed with MenQuadfi compared to those primed with MenACWY-PS. For more information, please refer to the Summary of Product Characteristics.
IB/0038/G	This was an application for a group of variations. 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 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	18/10/2024	n/a		
WS/2716/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.	05/09/2024	n/a		

	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.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS				
II/0030	Update of sections 4.5, 4.8 and 5.1 of the SmPC in order to update immunogenicity and safety information based on final results from study MEQ00071; this is a parallel, multi-center, multinational, randomized, active-controlled phase 3b immunogenicity and safety study of a quadrivalent meningococcal conjugate vaccine versus Nimenrix, and when administered alone or concomitantly with 9vHPV and Tdap-IPV vaccines in healthy adolescents aged 10 to 17 years. In addition, the MAH took the opportunity to introduce minor updates to the PI and to update the list of local representatives in the Package Leaflet. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	05/09/2024	13/11/2024	SmPC and PL	SmPC new text - Section 4.5 For ages 10 17 years, MenQuadfi can be co-administered with diphtheria, tetanus, pertussis (acellular, component) vaccine (adsorbed, reduced antigen(s) content) (Tdap), or Tdap and inactivated poliovirus vaccine (Tdap-IPV), and 4-valent human papillomavirus vaccine (recombinant, adsorbed) (4vHPV) or 9 valent HPV vaccine (9vHPV). However, the antibody responses to some of the antigens might be affected by the co-administration. The co-administration of MenQuadfi with Tdap-IPV and 9vHPV in children and adolescents aged 10-17 years resulted in lower GMTs and seroresponse rates for serogroup A, lower GMTs for serogroup W, lower responses to inactivated polio types 1 and 3, diphtheria, and anti-HPV types 6 and 58 (immune response assessed after the first dose of 9vHPV) compared to when MenQuadfi was given sequentially with Tdap-IPV and 9vHPV. The clinical implication of the observed reduced titre responses is unclear. Consideration might be given for sequential

					administration of MenQuadfi with Tdap-IPV and 9vHPV (e.g. for children and adolescents at higher risk). - Section 4.8 Children and adolescents aged 10-17 years of age were given either MenQuadfi alone (N=171) or MenQuadfi concomitantly with Tdap-IPV and the first dose of 9vHPV (N=116). The rates of injection site reaction pain at the 9vHPV injection site were higher when given concomitantly with Tdap-IPV and MenQuadfi (83.6%) compared to when Tdap-IPV and 9vHPV were given without MenQuadfi (67.3%). Overall, rates and intensity of adverse reactions were comparable between these two groups. - Section 5.1 MEQ00071 was conducted in subjects who were either meningococcal vaccine naïve or had been primed with MenC vaccines before two years of age. Seroprotection was evaluated 30 days following administration with either MenQuadfi alone, MenACWY TT alone, or MenQuadfi co-administrated with Tdap-IPV and 9vHPV. In an exploratory analysis in a non-random subset of participants (N=60), the immune response and protection rates were measured 6 and 30 days following co-administration of MenQuadfi with Tdap-IPV and 9vHPV. The proportion of subjects with seroprotection for serogroup A did not increase within 6 days, whereas most of the subjects had seroprotection against serogroups C, W and Y (>94%). After 30 days, protection rates in this subset were comparable to the full study population reported in table 8. Response in subjects according to MenC vaccination status The immunogenicity of serogroup C following administration of a single dose of MenQuadfi compared to a single dose of MenACWY-TT was assessed in both

					meningococcal vaccine naïve and MenC primed (before two years of age) subjects (MEQ00071). Overall, the post vaccination seroresponse and hSBA GMTs against serogroup C were higher in meningococcal vaccine naive subjects who received MenQuadfi than those who received MenACWY TT, with seroprotection rates also trending higher. No differences in antibody response were observed in MenC primed subjects between groups. For more information, please refer to the Summary of Product Characteristics.
IB/0035/G	This was an application for a group of variations. B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier 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	19/06/2024	13/11/2024	SmPC	
II/0031	Update of section 4.8 of the SmPC in order to add 'Hypersensitivity' and 'Anaphylaxis' to the list of adverse drug reactions (ADRs) with frequency 'not known' and 'very rare' respectively, based on a cumulative review of cases of hypersensitivity/allergic reaction (including anaphylaxis) following the request by PRAC in the Assessment Report for PSUSA/00010044/202304. The Package Leaflet is updated accordingly.	13/06/2024	13/11/2024	SmPC and PL	

	C.I.3.b - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Change(s) with new additional data submitted by the MAH				
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 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	11/04/2024	n/a		
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	21/02/2024	n/a		

	(excluding manufacturer for batch release)				
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 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	22/11/2023	13/11/2024	SmPC and PL	
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	16/11/2023	n/a		

	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				
WS/2495	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	13/07/2023	n/a		
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. 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	15/12/2022	31/03/2023	SmPC, Annex II and PL	The key SmPC text resulting from this variation read as 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

	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 new quality, preclinical, clinical or pharmacovigilance data				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 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 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	22/04/2022	31/03/2023	SmPC, Labelling and 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.	07/12/2021	04/04/2022	SmPC, Labelling and	

	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			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	02/09/2021	04/04/2022	SmPC and Annex II	Please refer to Scientific Discussion 'MenQuadfi-H-C-005084-II-0006'

	new quality, preclinical, clinical or pharmacovigilance data				
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 - 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	26/07/2021	04/04/2022	Annex II and PL	
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	12/05/2021	n/a		

	or addition) for the AS or a starting material/intermediate				
WS/2034	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.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	15/04/2021	n/a		
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	26/02/2021	n/a		

	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 site				