▼This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems.

AUSTRALIAN PRODUCT INFORMATION – MENQUADFI® (MENINGOCOCCAL (GROUPS A, C, Y, W) POLYSACCHARIDE TETANUS TOXOID CONJUGATE VACCINE) SOLUTION FOR INJECTION

1 NAME OF THE MEDICINE

Meningococcal (Groups A, C, Y, W) Polysaccharide Tetanus Toxoid Conjugate Vaccine

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 0.5 mL dose of vaccine contains:

- Meningococcal polysaccharide* Group A 10.0 microgram/dose
- Meningococcal polysaccharide* Group C 10.0 microgram/dose
- Meningococcal polysaccharide* Group Y 10.0 microgram/dose
- Meningococcal polysaccharide* Group W-135 10.0 microgram/dose

* Each of the four polysaccharides is conjugated to tetanus toxoid (approximately 55 microgram/dose)

MenQuadfi is a sterile solution of *Neisseria meningitidis* (*N. meningitidis*) purified capsular polysaccharides of groups A, C, W-135, and Y, individually conjugated to tetanus toxoid protein prepared from cultures of *Clostridium tetani*. No preservative or adjuvant is added during manufacture.

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

Solution for injection.

MenQuadfi is a clear, sterile, preservative-free solution.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

MenQuadfi is indicated for active immunisation for the prevention of invasive meningococcal disease caused by *Neisseria meningitidis* serogroups A, C, W and Y.

The use of MenQuadfi should be in accordance with official recommendations.

4.2 DOSE AND METHOD OF ADMINISTRATION

MenQuadfi should be administered as a 0.5 mL single dose injection by the intramuscular route only.

Primary Vaccination

- Individuals 12 months of age and older receive a single dose.

Booster Vaccination

- MenQuadfi may be given as a single booster dose to adolescents and adults who have previously been primed with meningococcal vaccine at least 4 years prior (see Section 5.1 Pharmacodynamic Properties).

Refer to official recommendations for further information regarding booster dosing.

Method of administration

MenQuadfi should be administered as a single 0.5 mL injection by intramuscular route into the deltoid region or anterolateral thigh, depending on the recipient's age and muscle mass.

No data are available to establish safety and efficacy of the vaccine using intradermal or subcutaneous routes of administration.

Refer to Section 4.5 Interactions with other medicines and other forms of interactions for concomitant administration with other vaccines.

The product is for single use only and must not be reused. Discard any remaining unused contents.

4.3 CONTRAINDICATIONS

MenQuadfi is contraindicated in anyone with a known systemic hypersensitivity reaction to any component of MenQuadfi or after previous administration of the vaccine or a vaccine containing the same components (See Section 2 Qualitative and quantitative composition and Section 6.1 List of excipients).

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Appropriate observation and medical treatment should always be readily available in case of an anaphylactic event following the administration of the vaccine.

Protection

As with any vaccine, vaccination with MenQuadfi may not protect all vaccine recipients.

MenQuadfi will not protect against *N meningitidis* serogroup B disease.

Immunisation with MenQuadfi does not substitute for routine tetanus immunisation.

Syncope

Syncope can occur following or even before any vaccination as a psychogenic response to the needle injection. Procedures should be in place to prevent falling and injury and to manage syncope.

Altered Immunocompetence

Reduced Immune Response

Some individuals with altered immunocompetence, including some individuals receiving immunosuppressant therapy, may have reduced immune responses to MenQuadfi.

Complement Deficiency

Individuals with certain complement deficiencies and individuals receiving treatment that inhibits terminal complement activation (for example, eculizumab) are at increased risk for invasive disease caused by *Neisseria meningitidis*, including invasive disease caused by serogroups A, C, W, and Y, even if they develop antibodies following vaccination with MenQuadfi.

Use in the elderly

Safety and efficacy of MenQuadfi administration in individuals older than 56 years of age have been established. Refer to Section 4.8 Adverse Effects and Section 5.1 Pharmacodynamic Properties for more information.

Paediatric use

Safety and efficacy of MenQuadfi administration in individuals less than 12 months of age have not been established.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Use with other vaccines

MenQuadfi should not be mixed with any other vaccine in the same vial or syringe.

If MenQuadfi needs to be given at the same time as another injectable vaccine(s), immunisation should be carried out on separate limbs.

MenQuadfi can be given concomitantly with any of the following vaccines:

- Measles-mumps-rubella vaccine (MMR) and varicella vaccine (V).
- Combined diphtheria - tetanus - acellular pertussis (DTPa) vaccines, including combination DTPa vaccines with hepatitis B, inactivated poliovirus or *Haemophilus influenzae* type b (HBV, IPV or Hib) such as DTPa-IPV-HB-Hib vaccine.
- 13-valent pneumococcal polysaccharide conjugate vaccine (PCV13).
- Diphtheria, Tetanus, Pertussis (acellular, component) Vaccine (adsorbed, reduced antigen(s) content) (dTpa).
- Human Papillomavirus Vaccine (Recombinant, adsorbed) (HPV).

The anti-pertussis responses following dTpa administered concomitantly with MenQuadfi and HPV versus dTpa administered concomitantly with HPV did not meet non-inferiority for the FHA, PRN, and FIM antigens. Because there are no established serological correlates of protection for pertussis, the clinical implications of the observed pertussis antigen responses are unknown.

(See Section 4.8 Adverse effects and Section 5.1 Pharmacodynamic properties – Concomitantly administered vaccine for safety and immunogenicity data)

Use with systemic immunosuppressive medicinal products

It may be expected that in individuals receiving immunosuppressive treatment or individuals with immunodeficiency, an adequate immune response may not be elicited.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

A developmental and reproductive toxicity study was performed in female rabbits. The animals were administered a full human dose (0.5 mL) of MenQuadfi intramuscularly on two occasions before mating and three occasions during gestation. There were no effects on mating performances or female fertility. No study was conducted on male fertility.

Use in pregnancy (Category B1)

Limited data are available on the use of MenQuadfi in pregnant women. However, no conclusions can be drawn regarding whether or not MenQuadfi is safe for use during pregnancy.

A developmental and reproductive toxicity study was performed in female rabbits. The animals were administered a full human dose of MenQuadfi (0.5 mL) intramuscularly on two occasions before mating and three occasions during gestation. The study showed no adverse effects on embryo-fetal development (including an evaluation of teratogenicity) or early post-natal development.

MenQuadfi should be used during pregnancy only if the potential benefits to the mother outweigh the potential risks, including those to the fetus.

Use in lactation

There are no available data on the presence of MenQuadfi in human milk, milk production, or the effects on the breastfed infant. No conclusions can be drawn regarding whether or not MenQuadfi is safe for use during breastfeeding.

MenQuadfi should be used during breastfeeding only if the potential benefits to the mother outweigh the potential risks, including those to the breastfed child.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

No studies on the effects of MenQuadfi on the ability to drive or use machines have been performed.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Clinical Trials

The safety of MenQuadfi in individuals 12 months of age and older is based on 7 pivotal clinical studies in which participants received either MenQuadfi alone (5,327 participants), MenQuadfi concomitantly with other vaccines (981 participants), the concomitant vaccines without MenQuadfi (590 participants), or a comparator meningococcal vaccine (2,898 participants).

Participants 12 through 23 months of age

The safety of MenQuadfi in participants 12 months through 23 months of age who were either meningococcal vaccine naive or who had received monovalent meningococcal C conjugate (MenC) vaccination during infancy was evaluated in a randomised, active-controlled, modified double-blind trial (MET51).

The rates of the solicited adverse reactions that occurred within seven days following MenQuadfi compared with a licensed quadrivalent meningococcal groups A, C, W-135 and Y Tetanus Toxoid conjugate vaccine (MenACWY-TT) are presented in Table 1.

Unsolicited injection-site reactions at the site of MenQuadfi injection included bruising, haematoma, induration, pruritus, and rash (0.3% each). Unsolicited systemic adverse events assessed as vaccine-related by the investigator more than once among recipient of MenQuadfi and which occurred at a rate of at least 1% during the 30 days post-vaccination included diarrhea (MenQuadfi 7.6%, MenACWY-TT 5.2%).

Table 1 - Frequency of Solicited Injection-Site Reactions and Systemic Reactions within 7 Days after Vaccination with MenQuadfi compared to MenACWY-TT, in Meningococcal Vaccine naive Participants 12 through 23 Months of Age

	MenQuadfi (N=303)		MenACWY-TT (N=306)	
Participants experiencing at least one:	n/M	%	n/M	%
General disorders and administration site conditions				
Local reactions				
Injection Site Tenderness	122/303	40.3	113/305	37.0
Injection Site Erythema	122/303	40.3	115/305	37.7
Injection Site Swelling	63/303	20.8	52/305	17.0
Systemic reactions				
Abnormal crying	106/303	35.0	110/305	36.1
Fever	29/303	9.6	38/304	12.5
Metabolism and nutrition disorders				
Appetite lost	90/303	29.7	93/305	30.5
Psychiatric disorders				
Irritability	144/303	47.5	127/305	41.6
Nervous system disorders				
Drowsiness	64/303	21.1	55/305	18.0
Gastrointestinal disorders				
Vomiting	21/303	6.9	13/305	4.3

n: number of participants experiencing the endpoint listed in the first column
M: number of participants with available data for the relevant endpoint
N: number of participants in the safety analysis set

Participants 2 through 9 years of age

The safety of MenQuadfi in participants 2 years through 9 years of age was evaluated in a randomised, active-controlled, modified double-blind trial (MET35).

The rates of the solicited adverse reactions that occurred within seven days following MenQuadfi compared with a licensed quadrivalent meningococcal groups A, C, W-135, and Y CRM_{197} protein conjugate vaccine (MenACWY-CRM) are presented in Table 2. Most adverse reactions were mild to moderate in severity.

The rates of local and systemic reactions among MenQuadfi recipients within 7 days after vaccination were generally comparable between the age subgroups 2-5 years and 6-9 years, with

the exception of headache, which occurred more frequently among the older children (2-5 years 7.0%, 6-9 years 18.0%).

Unsolicited injection-site reactions at the site of MenQuadfi injection included bruising (0.4%), induration (0.2%), and warmth (0.2%). Unsolicited systemic adverse events assessed as vaccine-related by the investigator more than once among recipient of MenQuadfi and which occurred at a rate of at least 1% during the 30 days post-vaccination included vomiting (MenQuadfi 2.4%, MenACWY-CRM 2.2%) and stomach pain (MenQuadfi 1.4%, MenACWY-CRM 1.0%).

Table 2 - Frequency of Solicited Injection-Site Reactions and Systemic Reactions within 7 Days after Vaccination with MenQuadfi compared to MenACWY-CRM, in Participants 2 through 9 Years of Age

	MenQuadfi (N=498)		MenACWY-CRM (N=494)	
Participants experiencing at least one:	n/M	%	n/M	%
General disorders and administration site conditions				
Local reactions				
Injection Site Pain	188/487	38.6	206/486	42.4
Injection Site Erythema	110/487	22.6	153/485	31.5
Injection Site Swelling	67/484	13.8	104/483	21.5
Systemic reactions				
Malaise	103/487	21.1	99/486	20.4
Fever	9/485	1.9	13/479	2.7
Nervous system disorders				
Headache	61/487	12.5	56/486	11.5
Musculoskeletal and connective tissue disorders				
Myalgia	98/487	23.0	112/486	23.0

n: number of participants experiencing the endpoint listed in the first column
M: number of participants with available data for the relevant endpoint
N: number of participants in the safety analysis set

Participants 10 through 17 years of age

The safety of MenQuadfi in participants 10 years through 17 years of age was evaluated in two clinical trials (MET43 and MET50): Study 1 (MET43) was a randomised, active-controlled, modified double-blind trial; Study 2 (MET50) was a randomised, controlled, open-label (the laboratory technicians were blinded to group assignment) concomitant trial. In the concomitant trial, MenQuadfi was given with dTpa and HPV. The comparator meningococcal vaccine was

either MenACWY-CRM (501 participants) or Meningococcal Groups A, C, Y, and W-135 Polysaccharide conjugated to Diphtheria Toxoid (MenACWY-DT) (323 participants).

The rates of the solicited adverse reactions that occurred within seven days following MenQuadfi alone compared with MenACWY-CRM and MenACWY-DT are presented in Table 3 respectively. Most adverse reactions were of mild to moderate severity.

Unsolicited injection-site reactions at the site of MenQuadfi injection when given alone and which occurred at a rate of at least 0.1% in either study MET50 or study MET43, included pruritus (0.6% and 0.7%), rash (0.2% and 0.2%), warmth (0.8% and 0.5%), bruising (0.2% and <0.1%) and induration (0.0% and 0.2%). There were no unsolicited systemic adverse events assessed as vaccine-related by the investigator any more than once among recipients of MenQuadfi and which occurred at a rate of at least 1% during the 30 days post-vaccination.

A few participants experienced dizziness or syncope within 30 minutes following vaccination (MenQuadfi 0.2% [dizziness], MenACWY-CRM 0.2% [syncope], MenACWY-DT 0.0%). These events were non-serious and spontaneously resolved on the same day.

Table 3 - Percentages of Solicited Injection-Site Reactions and Systemic Adverse Reactions within 7 Days after Vaccination with MenQuadfi or MenACWY-CRM in Individuals 10 through 17 Years of Age Study 1 and MenQuadfi or MenACWY-DT in Individuals 10 through 17 Years of Age Study 2

	Study 1				**Study 2**			
	MenQuadfi (N=503)		MenACWY-CRM (N=501)		MenQuadfi (N=1181)		MenACWY-DT (N=323)	
Participants experiencing at least one:	n/M	%	n/M	%	n/M	%	n/M	%
General disorders and administration site conditions								
Local Reactions								
Injection Site Pain§	224/496	45.2	209/492	42.5	404/1160	34.8	130/314	41.4
Injection Site Erythema¶	25/496	5.0	37/491	7.5	52/1160	4.5	14/314	4.5
Injection Site Swelling¶	27/496	5.4	32/491	6.5	47/1159	4.1	15/314	4.8
Systemic Reactions								
Malaise	129/496	26.0	130/492	26.4	225/1159	19.4	75/314	23.9

	Study 1				Study 2			
	MenQuadfi (N=503)		MenACWY-CRM (N=501)		MenQuadfi (N=1181)		MenACWY-DT (N=323)	
Participants experiencing at least one:	n/M	%	n/M	%	n/M	%	n/M	%
General disorders and administration site conditions								
Fever	7/494	1.4	6/488	1.2	8/1129	0.7	2/310	0.6
Nervous system disorders								
Headache	150/496	30.2	152/492	30.9	307/1158	26.5	88/314	28.0
Musculoskeletal and connective tissue disorders								
Myalgia	175/496	35.3	173/492	35.2	318/1159	27.4	98/314	31.2

n: number of participants experiencing the endpoint listed in the first column
M: number of participants with available data for the relevant endpoint
N: number of participants in the safety analysis set

Participants 18 through 55 years of age

The safety of MenQuadfi in participants 18 years through 55 years of age was evaluated in a randomised, active-controlled, modified double-blind trial (MET43).

The rates of the solicited adverse reactions that occurred within seven days following MenQuadfi compared with MenACWY-DT are presented in Table 4. Most adverse reactions were mild to moderate in severity.

Unsolicited injection-site reactions at the site of MenQuadfi injection with a frequency of at least 0.1% included pruritus (0.8%), warmth (0.3%), and mass (0.1%). There were no unsolicited systemic adverse events assessed as vaccine-related by the investigator more than once among recipient of MenQuadfi and which occurred at a rate of at least 1% during the 30 days post-vaccination.

A few participants experienced dizziness within 30 minutes following vaccination (MenQuadfi 0.3%, MenACWY-DT 0.3%). These events were non-serious and spontaneously resolved on the same day.

Table 4 - Frequency of Solicited Injection-Site Reactions and Systemic Reactions within 7 Days after Vaccination with MenQuadfi compared to MenACWY-DT, in Participants 18 through 55 Years of Age

	MenQuadfi (N=1495)		MenACWY-DT (N=312)	
Participants experiencing at least one:	n/M	%	n/M	%
General disorders and administration site conditions				
Local reactions				
Injection Site Pain	611/1458	41.9	105/300	35.0
Injection Site Erythema	75/1459	5.1	11/300	3.7
Injection Site Swelling	63/1458	4.3	10/298	3.4
Systemic reactions				
Malaise	334/1459	22.9	57/301	18.9
Fever	20/1441	1.4	5/297	1.7
Nervous system disorders				
Headache	423/1460	29.0	83/301	27.6
Musculoskeletal and connective tissue disorders				
Myalgia	520/1460	35.6	94/301	31.2

n: number of participants experiencing the endpoint listed in the first column
M: number of participants with available data for the relevant endpoint
N: number of participants in the safety analysis set

Participants 56 years of age and older

The safety of MenQuadfi in participants 56 years of age and older was evaluated in clinical trial (MET49).

The rates of the solicited adverse reactions that occurred within seven days following MenQuadfi compared with Meningococcal Polysaccharide Vaccine, Groups A, C, Y, and W combined (MenACWY-PS) in study MET49 are presented in Table 5. Most adverse reactions were mild to moderate in severity.

The rates of local and systemic reactions among MenQuadfi within 7 days after vaccination were generally higher in the 56-64 year age subgroup compared with the 65 years of age and older subgroup.

Unsolicited injection-site reactions at the site of MenQuadfi injection included pruritus (1.8%), warmth (0.2%) and ecchymosis (0.2%). There were no unsolicited systemic adverse events assessed as vaccine-related by the investigator more than once among recipient of MenQuadfi and which occurred at a rate of at least 1% during the 30 days post-vaccination.

Table 5 - Frequency of Solicited Injection-Site Reactions and Systemic Reactions within 7 Days after Vaccination with MenQaudfi compared to MenACWY-PS, in Participants 56 Years of Age and Older

	MenQuadfi (N=448)		MenACWY-PS (N=453)	
Participants experiencing at least one:	n/M	%	n/M	%
General disorders and administration site conditions				
Local reactions				
Injection Site Pain	113/443	25.5	43/450	9.6
Injection Site Erythema	23/443	5.2	0/451	0.0
Injection Site Swelling	20/443	4.5	0/451	0.0
Systemic reactions				
Malaise	64/442	14.5	51/451	11.3
Fever	9/436	2.1	2/449	0.4
Nervous system disorders				
Headache	84/442	19.0	66/451	14.6
Musculoskeletal and connective tissue disorders				
Myalgia	97/442	21.9	69/451	15.3

n: number of participants experiencing the endpoint listed in the first column
M: number of participants with available data for the relevant endpoint
N: number of participants in the safety analysis set

Individuals 15 years of age and older who have been previously vaccinated with either MenACWY-DT or MenACWY-CRM

The safety of MenQuadfi in previously vaccinated participants 15 years of age and older was evaluated in a randomised, active-controlled, modified double-blind (MET56) trial. Participants had received a quadrivalent meningococcal conjugate vaccine 4 to 10 years previously.

The rates of the solicited adverse reactions that occurred within seven days following MenQuadfi compared with MenACWY-DT are presented in Table 6. Most adverse reactions were mild to moderate in severity.

Table 6 - Frequency of Solicited Injection-Site Reactions and Systemic Reactions within 7 Days after Vaccination with MenQuadfi compared to MenACWY-DT, in Participants 15 Years of Age and Older

	MenQuadfi (N=402)		MenACWY-DT (N=407)	
Participants experiencing at least one:	n/M	%	n/M	%
General disorders and administration site conditions				
Local reactions				
Injection Site Pain	178/398	44.7	196/402	48.8
Injection Site Erythema	20/398	5.0	6/402	1.5
Injection Site Swelling	16/398	4.0	3/402	0.7
Systemic reactions				
Malaise	110/398	27.6	108/402	26.9
Fever	0/390	0.0	2/395	0.5
Nervous system disorders				
Headache	151/398	37.9	134/402	33.3
Musculoskeletal and connective tissue disorders				
Myalgia	146/398	36.7	156/402	38.8

n: number of participants experiencing the endpoint listed in the first column
M: number of participants with available data for the relevant endpoint
N: number of participants in the safety analysis set

Concomitant use with MMR and V for ages 12-23 months

The safety of MenQuadfi administered concomitantly with MMR and V was evaluated in a randomised, controlled, open-label (the laboratory technicians were blinded to group assignment) trial (MET57).

The rates of local reactions at each of the injection sites were comparable when MenQuadfi was given concomitantly with MMR and V, MenQuadfi was given alone, and MMR and V were given without MenQuadfi.

The overall rates of solicited systemic reactions reported for participants receiving MenQuadfi + MMR + V (46.6%) were comparable to rates among participants who received MMR + V without MenQuadfi (43.2%), or MenQuadfi alone (54.3%). In the three groups the most common solicited systemic reactions were irritability (MenQuadfi + MMR + V, 23.8%; MMR +V, 26.3%; MenQuadfi alone, 24.5%), abnormal crying (MenQuadfi + MMR + V, 18.5%; MMR +V, 18.9%; MenQuadfi alone, 27.7%), and appetite lost (MenQuadfi + MMR + V, 21.2%; MMR +V, 13.7%; MenQuadfi alone, 23.4%).

Concomitant use with PCV13 for ages 12-23 months

The safety of MenQuadfi administered concomitantly with PCV13 as evaluated in a randomised, open-label (the laboratory technicians were blinded to group assignment) trial (MET57).

The rates of local reactions at the PCV13 injection sites tended to be higher when MenQuadfi was given concomitantly with PCV13 compared with PCV13 given without MenQuadfi.

The overall rates of solicited systemic reactions reported for participants receiving MenQuadfi + PCV13 (20.0%) were comparable to rates among participants who received MenQuadfi alone (19.0%). The overall rate of solicited systemic reactions was lower for participants receiving PCV13 without MenQuadfi (10.1%). In the three groups the most common systemic reactions were irritability (MenQuadfi + PCV13, 13.0%; PCV13, 9.1%; MenQuadfi alone, 16.0%), appetite lost (MenQuadfi + PCV13, 9.5%; PCV13, 7.1%; MenQuadfi alone, 12.0%), and drowsiness (MenQuadfi + PCV13, 12.5%; PCV13, 4.0%; MenQuadfi alone, 6.0%).

Concomitant use with dTpa and HPV for ages 10-17 years

The safety of MenQuadfi administered concomitantly with dTpa and HPV was evaluated in a randomised, controlled, open-label (the laboratory technicians were blinded to group assignment) trial (MET50).

The overall rate of solicited systemic reactions was higher when MenQuadfi was given concomitantly with dTpa and HPV (70.6%) than when MenQuadfi was given alone (52.0%) and comparable to when dTpa and HPV were given without MenQuadfi (65.9%). In the three groups the most common solicited systemic reactions were myalgia (MenQuadfi + dTpa + HPV, 61.3%; dTpa +HPV, 55.4%; MenQuadfi alone, 35.3%) and headache (MenQuadfi + dTpa + HPV, 33.8%; dTpa + HPV, 29%; MenQuadfi alone, 30.2%). The rates of local reactions at each of the injection sites were comparable when MenQuadfi was given concomitantly with dTpa and HPV, MenQuadfi was given alone, and dTpa and HPV were given without MenQuadfi.

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems (Australia) or https://nzphvc.otago.ac.nz/reporting/ (New Zealand).

4.9 OVERDOSE

For general advice on overdose management, contact the Poisons Information Centre, telephone number 13 11 26 (Australia) or the National Poisons Centre, 0800 POISON or 0800 764 766 (New Zealand).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: meningococcal vaccine, ATC code: J07AH08

Mechanism of action

Invasive meningococcal disease (IMD) is caused by the bacterium *N. meningitidis*, a gram-negative diplococcus found exclusively in humans. The presence of bactericidal anti-capsular meningococcal antibodies has been associated with protection from IMD. MenQuadfi induces the production of bactericidal antibodies specific to the capsular polysaccharides of *N. meningitidis* serogroups A, C, W, and Y.

Clinical trials

The efficacy of a single dose of MenQuadfi for primary vaccination in toddlers (12 – 23 months of age), children and adolescents (2 – 17 years of age), adults (18 – 55 years of age) and older adults (56 years and above) was assessed in 6 pivotal studies; the efficacy of a single dose of MenQuadfi for booster vaccination (ages 15 years and above) was assessed in one pivotal study. All 7 studies were randomised, parallel-group, multi-centre studies. Six out of 7 studies were active controlled. Clinical study comparators were MenACWY-TT, MenACWY-CRM, MenACWY-DT, and MenACWY-PS. Two out of 7 studies were open-label. The other 5 studies were modified, double-blind.

Serum was collected at baseline and 30 days post vaccination to measure antibodies with a serum bactericidal assay using human complement (hSBA). MenQuadfi immune response was assessed primarily by three criteria based upon the hSBA responses unless specified otherwise.

- Seroprotection rates– Defined as the proportions of participants with a post-vaccination hSBA ≥1:8.
- Vaccine Seroresponse rates – Defined as the proportions of participants with an hSBA pre-vaccination titre < 1:8 who achieved a post-vaccination titre ≥ 1:16 or participants with a pre-vaccination titre ≥ 1:8 who achieved a post-vaccination titre at least 4-fold greater than the pre-vaccination titre.
- Geometric mean titres (GMTs).

Non-inferiority of immune responses was consistently demonstrated between MenQuadfi and comparator vaccines for all four serogroups across all ages, based on percentages of meningococcal naive participants and individuals receiving the vaccine as booster achieving hSBA vaccine seroresponse at Day 30 compared to baseline (ages 2 years and above) or percentages of participants achieving seroprotection (hSBA ≥ 1:8) at Day 30 (age 12-23 months).

Overall, immunogenicity results using rabbit complement (rSBA) to measure SBA activity were consistent with what was observed with hSBA assay.

Participants 12 to 23 month of age

Efficacy in participants 12 through 23 months of age was evaluated in 2 clinical studies (MET51 and MET57).

MET51 was conducted in participants who were either meningococcal vaccine naive or had been primed with monovalent meningococcal C vaccines (MenC-TT or MenC-CRM) in the first year of life.

Non-inferiority of immune response, based on percentage of subjects achieving a post-vaccination hSBA titre ≥ 1:8 at Day 30 regardless of their meningococcal vaccine background, was demonstrated for MenQuadfi versus MenACWY-TT vaccine for all serogroups.

Non-inferiority of immune response, based on percentage of subjects achieving a post-vaccination hSBA titre ≥ 1:8 at Day 30 in meningococcal vaccine naive toddlers, was demonstrated for MenQuadfi versus MenACWY-TT vaccine for all serogroups (see Table 7).

The point estimates of the immune response endpoints (with corresponding 95% confidence intervals [CIs]) and the differences or ratios observed between the two vaccines administered (with corresponding 95% CIs) in naive toddlers are summarised in Table 7 below.

Table 7 - Comparison of Bactericidal Antibody Responses to MenQuadfi and MenACWY-TT vaccine 30 Days after Vaccination of Meningococcal Vaccine naive Participants 12 through 23 Months of Age (MET51)

Endpoint by Serogroup	MenQuadfi (95% CI)	MenACWY-TT (95% CI)	% difference MenQuadfi - MenACWY-TT (95% CI)	MenQuadfi / MenACWY-TT (95% CI)
A				
% ≥1:8 (Seroprotection)§	90.8 (86.9; 93.8) N=293	89.5 (85.4; 92.7) N=295	1.3 (-3.60; 6.20)	
% Seroresponse	76.8 (71.5; 81.5) N=293	72.5 (67.1; 77.6) N=295	4.2 (-2.78;11.2)	
hSBA GMT	28.7 (25.2; 32.6) N=293	28.0 (24.4; 32.1) N=295		1.03 (0.850; 1.24)
C				
% ≥1:8 (Seroprotection)§	99.3 (97.6; 99.9) N=293	81.4 (76.4; 85.6) N=295	18.0 (13.6; 22.8)	
% Seroresponse	98.3 (96.1; 99.4) N=293	71.5 (66.0; 76.6) N=295	26.8 (21.4; 32.3)	
hSBA GMT	436 (380; 500) N=293	26.4 (22.5; 31.0) N=295		16.5 (13.4; 20.4)

Endpoint by Serogroup	MenQuadfi (95% CI)	MenACWY-TT (95% CI)	% difference MenQuadfi - MenACWY-TT (95% CI)	MenQuadfi / MenACWY-TT (95% CI)
W				
% ≥1:8 (Seroprotection)§	83.6 (78.9; 87.7) N=293	83.4 (78.7; 87.5) N=296	0.2 (-5.85; 6.18)	
% Seroresponse	67.6 (61.9; 72.9) N=293	66.6 (60.9; 71.9) N=296	1.0 (-6.54; 8.57)	
hSBA GMT	22.0 (18.9; 25.5) N=293	16.4 (14.4; 18.6) N=296		1.34 (1.10; 1.63)
Y				
% ≥1:8 (Seroprotection)§	93.2 (89.7; 95.8) N=293	91.6 (87.8; 94.5) N=296	1.6 (-2.76; 6.03)	
% Seroresponse	81.9 (77.0; 86.1) N=293	79.1 (74.0; 83.5) N=296	2.9 (-3.56; 9.25)	
hSBA GMT	38.0 (33.0; 43.9) N=293	32.2 (28.0; 37.0) N=296		1.18 (0.970; 1.44)

N: number of participants in per-protocol analysis set with valid serology results
95% CI of the single proportion calculated from the exact binomial method.
95% CI of the difference calculated from the Wilson Score method without continuity correction.
§Overall non-inferiority would be demonstrated if the lower limit of the 2-sided 95% CI is > -10% for all four serogroups.

MET57 was conducted in meningococcal vaccine naive toddlers 12 through 23 months of age to assess the immunogenicity and safety of concomitant administration of MenQuadfi with paediatric vaccines (MMR+V, DTPa-IPV-HB-Hib or PCV). Overall, the post vaccination hSBA seroprotection rates in participants who received MenQuadfi was high for all serogroups (between 88.9% and 100%), and GMTs were higher for serogroup C than for serogroups A, W and Y.

Participants 2 through 9 years of age

Efficacy in participants 2 through 9 years of age was evaluated in study MET35 (stratified by ages 2 through 5 and 6 through 9 years) comparing seroresponses following administration of either MenQuadfi or MenACWY-CRM.

Overall for participants 2 through 9 years of age, immune non-inferiority, based on hSBA seroresponse, was demonstrated for MenQuadfi as compared to MenACWY-CRM for all four serogroups. The post vaccination hSBA seroprotection rates and GMTs for serogroups C, W, and Y were higher in participants who received MenQuadfi than those who received MenACWY-CRM. For Serogroup A, the post vaccination hSBA seroprotection rates and GMTs were similar in participants who received MenQuadfi than those who received MenACWY-CRM. The point estimates of the immune response endpoints (with corresponding 95% confidence intervals [CIs])

and the differences or ratios observed between the two vaccines administered (with corresponding 95% CIs) in naive children are summarised in Table 8 below.

Table 8 - Comparison of Bactericidal Antibody Response to MenQuadfi and MenACWY-CRM 30 Days after Vaccination of Participants 2 through 5 years and 6 through 9 Years of Age (MET35)

Endpoint by Serogroup	MenQuadfi (95% CI)	MenACWY-CRM (95% CI)	% difference MenQuadfi - MenACWY-CRM (95% CI)	MenQuadfi / MenACWY-CRM (95% CI)
2-5 years				
A				
% ≥1:8 (Seroprotection)	84.6 (79.3; 89.1) N=228	76.5 (70.3; 81.9) N=221	8.2 (0.9; 15.5)	
% Seroresponse §	52.4 (45.7; 59.1) N=227	44.8 (38.1; 51.6) N=221	7.6 (-1.6; 16.7)	
hSBA GMT	21.6 (18.2; 25.5) N=228	18.9 (15.5; 23.0) N=221		1.14 (0.883; 1.47)
C				
% ≥1:8 (Seroprotection)	97.4 (94.4; 99.0) N=229	64.6 (57.9; 70.8) N=223	32.8 (26.1; 39.4)	
% Seroresponse §	94.3 (90.5; 96.9) N=229	43.2 (36.6; 50.0) N=222	51.1 (43.5; 57.8)	
hSBA GMT	208 (175; 246) N=229	11.9 (9.79; 14.6) N=223		17.4 (13.4; 22.6)
W				
% ≥1:8 (Seroprotection)	90.8 (86.3; 94.2) N=229	80.6 (74.8; 85.6) N=222	10.2 (3.8; 16.7)	
% Seroresponse §	73.8 (67.6; 79.4) N=229	61.3 (54.5; 67.7) N=222	12.5 (3.9; 20.9)	
hSBA GMT	28.8 (24.6; 33.7) N=229	20.1 (16.7; 24.2) N=222		1.43 (1.12; 1.83)
Y				
% ≥1:8 (Seroprotection)	97.8 (95.0; 99.3) N=229	86.9 (81.8; 91.1) N=222	10.9 (6.1; 16.1)	
% Seroresponse §	88.2 (83.3; 92.1) N=229	77.0 (70.9; 82.4) N=222	11.2 (4.2; 18.1)	

Endpoint by Serogroup	MenQuadfi (95% CI)	MenACWY-CRM (95% CI)	% difference MenQuadfi - MenACWY-CRM (95% CI)	MenQuadfi / MenACWY-CRM (95% CI)
hSBA GMT	49.8 (43.0; 57.6) N=229	36.1 (29.2; 44.7) N=222		1.38 (1.07; 1.78)
6-9 years				
A				
% ≥1:8 (Seroprotection)	88.2 (83.2; 92.0) N=228	81.9 (76.3; 86.5) N=237	6.3 (-0.2; 12.8)	
% Seroresponse §	58.3 (51.6; 64.8) N=228	50.6 (44.1; 57.2) N=237	7.7 (-1.3; 16.6)	
hSBA GMT	28.4 (23.9; 33.8) N=228	26.8 (22.0; 32.6) N=237		1.06 (0.816; 1.38)
C				
% ≥1:8 (Seroprotection)	98.3 (95.6; 99.5) N=229	69.5 (63.2; 75.3) N=236	28.8 (22.6; 35.0)	
% Seroresponse §	96.1 (92.7; 98.2) N=229	52.1 (45.5; 58.6) N=236	44.0 (36.8; 50.6)	
hSBA GMT	272 (224; 330) N=229	23.7 (18.2; 31.0) N=236		11.5 (8.24; 16.0)
W				
% ≥1:8 (Seroprotection)	98.7 (96.2; 99.7) N=229	91.6 (87.3; 94.8) N=237	7.1 (3.3; 11.5)	
% Seroresponse §	83.8 (78.4; 88.4) N=229	66.7 (60.3; 72.6) N=237	17.2 (9.4; 24.7)	
hSBA GMT	48.9 (42.5; 56.3) N=229	33.6 (28.2; 40.1) N=237		1.45 (1.16; 1.82)
Y				
% ≥1:8 (Seroprotection)	99.1 (96.9; 99.9) N=229	94.5 (90.8; 97.0) N=237	4.6 (1.4; 8.3)	
% Seroresponse §	94.8 (91.0; 97.3) N=229	81.4 (75.9; 86.2) N=237	13.3 (7.6; 19.2)	
hSBA GMT	95.1 (80.2; 113) N=229	51.8 (42.5; 63.2) N=237		1.84 (1.41; 2.38)

N: number of participants in per-protocol analysis set with valid serology results
95% CI of the single proportion calculated from the exact binomial method.

95% CI of the difference calculated from the Wilson Score method without continuity correction.
§Overall non-inferiority would be demonstrated if the lower limit of the 2-sided 95% CI is > -10% for all four serogroups.

Participants 10 through 17 years of age

Efficacy in participants aged 10 through 17 years of age was evaluated in two studies comparing seroresponses following administration of MenQuadfi with either MenACWY-CRM (MET50) or MenACWY-DT (MET43).

MET50 was conducted in meningococcal vaccine naive male and female participants and evaluated seroresponses following administration with either MenQuadfi alone; MenACWY-CRM alone; MenQuadfi co-administered with dTpa and HPV; or dTpa and HPV alone.

Overall immune non-inferiority, based on hSBA seroresponse, was demonstrated for MenQuadfi as compared to MenACWY-CRM for all four serogroups. The post vaccination hSBA seroprotection rates for serogroups A, C, W, and Y were higher in participants who received MenQuadfi than those who received MenACWY-CRM. The post vaccination hSBA GMTs for serogroups C, W, and Y were higher in participants who received MenQuadfi than those who received MenACWY-CRM and comparable for serogroup A. The point estimates of the immune response endpoints (with corresponding 95% confidence intervals) and the differences or ratio observed between the two vaccines administered (with corresponding 95% confidence intervals) in naive adolescents is summarised in Table 9 below.

Table 9 - Comparison of Bactericidal Antibody Responses to MenQuadfi and MenACWY-CRM 30 Days after Vaccination of Participants 10 through 17 Years of Age (MET50)

Endpoint[1] by Serogroup	MenQuadfi (95% CI)	MenACWY-CRM (95% CI)	% difference MenQuadfi - MenACWY-CRM (95% CI)	MenQuadfi / MenACWY-CRM (95% CI)
A				
% ≥1:8 (Seroprotection)	93.5 (90.9; 95.6) N=463	82.8 (79.0; 86.1) N=464	10.8 (6.7; 14.9)	
% Seroresponse§	75.6 (71.4; 79.4) N=463	66.4 (61.9; 70.7) N=464	9.2 (3.4; 15.0)	
hSBA GMT	44.1 (39.2; 49.6) N=463	35.2 (30.3; 41.0) N=464		1.25 (1.033; 1.517)
C				
% ≥1:8 (Seroprotection)	98.5 (96.9; 99.4) N=462	76.0 (71.9; 79.8) N=463	22.5 (18.5; 26.6)	

Endpoint[1] by Serogroup	MenQuadfi (95% CI)	MenACWY-CRM (95% CI)	% difference MenQuadfi - MenACWY-CRM (95% CI)	MenQuadfi / MenACWY-CRM (95% CI)
% Seroresponse§	97.2 (95.2; 98.5) N=462	72.6 (68.3; 76.6) N=463	24.6 (20.3; 29.0)	
hSBA GMT	387 (329; 456) N=462	51.4 (41.2; 64.2) N=463		7.53 (5.717; 9.919)
W				
% ≥1:8 (Seroprotection)	99.1 (97.8; 99.8) N=463	90.7 (87.7; 93.2) N=464	8.4 (5.7; 11.4)	
% Seroresponse§	86.2 (82.7; 89.2) N=463	66.6 (62.1; 70.9) N=464	19.6 (14.2; 24.8)	
hSBA GMT	86.9 (77.8; 97.0) N=463	36.0 (31.5; 41.0) N=464		2.42 (2.035; 2.868)
Y				
% ≥1:8 (Seroprotection)	97.2 (95.2; 98.5) N=463	83.2 (79.5; 86.5) N=464	14.0 (10.3; 17.9)	
% Seroresponse§	97.0 (95.0; 98.3) N=462	80.8 (76.9; 84.3) N=464	16.2 (12.3; 20.2)	
hSBA GMT	75.7 (66.2; 86.5) N=463	27.6 (23.8; 32.1) N=464		2.74 (2.244; 3.351)

N: number of participants in per-protocol analysis set with valid serology results
95% CI of the single proportion calculated from the exact binomial method.
95% CI of the difference calculated from the Wilson Score method without continuity correction.
§Overall non-inferiority would be demonstrated if the lower limit of the 2-sided 95% CI is > -10% for all four serogroups.
[1]Seroresponse rate (primary end point) for each serogroup: post-vaccination hSBA titers ≥1:8 for participants with pre-vaccination hSBA titers < 1:8 or at least a 4-fold increase in hSBA titers from pre to post-vaccination for participants with pre-vaccination hSBA titers ≥1:8.

Study MET43 was performed to evaluate the efficacy of MenQuadfi compared to MenACWY-DT in children, adolescents and adults (10-55 years of age).

In MET 43, immune non-inferiority, based on hSBA seroresponse, was demonstrated for MenQuadfi as compared to MenACWY-DT for all four serogroups. The post vaccination hSBA seroprotection rates and GMTs for serogroups A, C, W, and Y were higher in participants who received MenQuadfi than those who received MenACWY-DT. The point estimates of the immune endpoints (with corresponding 95% confidence intervals) and the differences or ratio observed between the two vaccines administered (with corresponding 95% confidence intervals) in naive adolescents is summarised in Table 10 below.

Table 10 - Comparison of Bactericidal Antibody Response to MenQuadfi and MenACWY-DT 30 Days after Vaccination of Participants 10 through 17 Years of Age (MET43)

Endpoint by Serogroup	MenQuadfi (95% CI)	MenACWY-DT (95% CI)	% difference MenQuadfi - MenACWY-DT (95% CI)	MenQuadfi / MenACWY-DT (95% CI)
A				
% ≥1:8 (Seroprotection)	96.2 (94.9; 97.2) N=1,097	89.0 (84.9; 92.3) N=300	7.2 (3.8; 11.3)	
% Seroresponse§	74.0 (71.3; 76.6) N=1,097	55.3 (49.5; 61.0) N=300	18.7 (12.5; 24.9)	
hSBA GMT	78 (71.4; 85.2) N=1,097	44.2 (36.4; 53.7) N=300		1.76 (1.42; 2.18)
C				
% ≥1:8 (Seroprotection)	98.5 (97.5; 99.1) N=1,098	74.7 (69.3; 79.5) N=300	23.8 (19.1; 29.0)	
% Seroresponse§	95.6 (94.2; 96.8) N=1,097	53.3 (47.5; 59.1) N=300	42.3 (36.6; 48.0)	
hSBA GMT	504 (456; 558) N=1,098	44.1 (33.7; 57.8) N=300		11.4 (8.57; 15.2)
W				
% ≥1:8 (Seroprotection)	98.3 (97.3; 99.0) N=1,097	93.7 (90.3; 96.1) N=300	4.6 (2.2; 8.0)	
% Seroresponse§	84.5 (82.2; 86.6) N=1,097	72.0 (66.6; 77.0) N=300	12.5 (7.22; 18.2)	
hSBA GMT	97.2 (88.3; 107) N=1,097	59.2 (49.1; 71.3) N=300		1.64 (1.33; 2.03)
Y				
% ≥1:8 (Seroprotection)	99.1 (98.3; 99.6) N=1,097	94.3 (91.1; 96.7) N=300	4.8 (2.5; 8.0)	
% Seroresponse§	95.6 (94.2; 96.8) N=1,097	85.7 (81.2; 89.4) N=300	10.0 (6.18; 14.5)	
hSBA GMT	208 (189; 228) N=1,097	80.3 (65.6; 98.2) N=300		2.59 (2.07; 3.23)

N: number of participants in per-protocol analysis set with valid serology results
95% CI of the single proportion calculated from the exact binomial method.
95% CI of the difference calculated from the Wilson Score method without continuity correction.
§The overall non-inferiority would be demonstrated if the lower limit of the 2-sided 95% CI is > -10% for all four serogroups.

Participants 18 through 55 years of age

Efficacy in participants from 18 through 55 years of age was evaluated in study MET43 comparing MenQuadfi to MenACWY-DT. Immune non-inferiority, based on hSBA seroresponse, was demonstrated for MenQuadfi as compared to MenACWY-DT for all four serogroups. The post vaccination hSBA seroprotection rates and GMTs for serogroups A, C, W, and Y were higher in participants who received MenQuadfi than those who received MenACWY-DT. The point estimates of the immune endpoints (with corresponding 95% confidence intervals) and the differences or ratio observed between the two vaccines administered (with corresponding 95% confidence intervals) in naive adults is summarised in Table 11 below.

Table 11 - Comparison of Bactericidal Antibody Responses to MenQuadfi and MenACWY-DT 30 Days after Vaccination of Participants 18 through 55 Years of Age (MET43)

Endpoint by Serogroup	MenQuadfi (95% CI)	MenACWY-DT (95% CI)	% difference MenQuadfi - MenACWY-DT (95% CI)	MenQuadfi / MenACWY-DT (95% CI)
A				
% ≥1:8 (Seroprotection)	93.5 (92.1; 94.8) N=1,408	88.1 (83.8; 91.5) N=293	5.5 (2.0; 9.9)	
% Seroresponse§	73.5 (71.2; 75.8) N=1,406	53.9 (48.0; 59.7) N=293	19.6 (13.5; 25.8)	
hSBA GMT	106 (97.2; 117) N=1,408	52.3 (42.8; 63.9) N=293		2.03 (1.63; 2.53)
C				
% ≥1:8 (Seroprotection)	93.5 (92.0; 94.7) N=1,408	77.8 (72.6; 82.4) N=293	15.7 (11.0; 20.9)	
% Seroresponse§	83.4 (81.4; 85.3) N=1,406	42.3 (36.6; 48.2) N=293	41.1 (35.0; 46.9)	
hSBA GMT	234 (210; 261) N=1,408	37.5 (29.0; 48.5) N=293		6.24 (4.77; 8.16)
W				
% ≥1:8 (Seroprotection)	94.5 (93.2; 95.7) N=1,410	80.2 (75.2; 84.6) N=293	14.3 (10.0; 19.4)	
% Seroresponse§	77.0 (74.7; 79.2) N=1,408	50.2 (44.3; 56.0) N=293	26.8 (20.7; 32.9)	
hSBA GMT	75.6 (68.7; 83.2) N=1,410	33.2 (26.3; 42.0) N=293		2.27 (1.77; 2.93)

Endpoint by Serogroup	MenQuadfi (95% CI)	MenACWY-DT (95% CI)	% difference MenQuadfi - MenACWY-DT (95% CI)	MenQuadfi / MenACWY-DT (95% CI)
Y				
% ≥1:8 (Seroprotection)	98.6 (97.8; 99.1) N=1,410	81.2 (76.3; 85.5) N=293	17.4 (13.2; 22.2)	
% Seroresponse§	88.1 (86.3; 89.8) N=1,408	60.8 (54.9; 66.4) N=293	27.4 (21.7; 33.3)	
hSBA GMT	219 (200; 239) N=1,410	54.6 (42.3; 70.5) N=293		4.00 (3.05; 5.24)

N: number of participants in per-protocol analysis set with valid serology results.
95% CI of the single proportion calculated from the exact binomial method.
95% CI of the difference calculated from the Wilson Score method without continuity correction.
§The overall non-inferiority would be demonstrated if the lower limit of the 2-sided 95% CI is > -10% for all four serogroups

Participants 56 years of age and above

Immunogenicity in adults ≥ 56 years of age was assessed in study MET49 comparing the immunogenicity of MenQuadfi to MenACWY-PS.

In study MET49, the overall mean age of participants who received MenQuadfi was 66.9 years. The age range of participants was 56 through 89.8 years of age. The immune response to MenQuadfi based on hSBA seroresponse was non-inferior to that of MenACWY-PS for all four serogroups. The percentages of participants with hSBA titres ≥ 1:8 increased from baseline for all serogroups and in both groups (see Table 12).

In participants 56 through 64 years of age, participants ≥ 65 years, participants 65 through 74 years and participants ≥ 75 years of age, seroprotection rates were comparable between MenQuadfi and MenACWY-PS for serogroup A and higher for serogroups C, Y and W in participants who received MenQuadfi than those who received MenACWY-PS. In participants 56 through 64 years of age and ≥ 65 years the GMTs were higher for all serogroups in those who received MenQuadfi than those who received MenACWY-PS. In participants 65 through 74 years of age, the GMTs were higher for serogroups C, Y and W, and comparable for serogroup A in those who received MenQuadfi than those who received MenACWY-PS. In participants ≥ 75 years of age the GMTs were higher for serogroup C, and comparable for serogroups A, Y and W in those who received MenQuadfi than those who received MenACWY-PS.

Overall for adults ≥ 56 years of age, immune non-inferiority, based on hSBA seroresponse, was demonstrated for MenQuadfi as compared to MenACWY PS for all four serogroups. The post vaccination hSBA GMTs for serogroups A, C, W, and Y were higher in participants who received MenQuadfi than those who received MenACWY-PS. The post vaccination hSBA seroprotection

rates for serogroups C, W, and Y were higher in participants who received MenQuadfi than those who received MenACWY-PS. The point estimates of the immune endpoints (with corresponding 95% confidence intervals) and the differences or ratio observed between the two vaccines administered (with corresponding 95% confidence intervals) in naive older adults is summarised in Table 12 below.

Table 12 - Comparison of Bactericidal Antibody Responses to MenQuadfi and MenACWY-PS in naive Older Adults and Elderly 30 Days after Vaccination (MET49)

Serogroup Endpoint	MenQuadfi (95% CI)	MenACWY-PS (95% CI)	% difference MenQuadfi – MenACWY-PS (95% CI)	MenQuadfi / MenACWY-PS (95% CI)
A				
% ≥1:8 (Seroprotection)	89.4 (86.1; 92.1) N=433	84.2 (80.4; 87.5) N=431	5.2 (0.6; 9.7)	
% Seroresponse§	58.2 (53.4; 62.9) N=433	42.5 (37.7; 47.3) N=431	15.7 (9.08; 22.2)	
hSBA GMT	55.1 (46.8; 65.0) N=433	31.4 (26.9; 36.7) N=431		1.75 (1.40; 2.20)
C				
% ≥1:8 (Seroprotection)	90.1 (86.9; 92.7) N=433	71.0 (66.5; 75.2) N=431	19.1 (13.9; 24.2)	
% Seroresponse§	77.1 (72.9; 81.0) N=433	49.7 (44.8; 54.5) N=431	27.5 (21.2; 33.5)	
hSBA GMT	101 (83.8; 123) N=433	24.7 (20.7; 29.5) N=431		4.10 (3.16; 5.33)
W				
% ≥1:8 (Seroprotection)	77.4 (73.1; 81.2) N=433	63.1 (58.4; 67.7) N=431	14.3 (8.2; 20.2)	
% Seroresponse§	62.6 (57.8; 67.2) N=433	44.8 (40.0; 49.6) N=431	17.8 (11.2; 24.2)	
hSBA GMT	28.1 (23.7; 33.3) N=433	15.5 (13.0; 18.4) N=431		1.81 (1.42; 2.31)
Y				
% ≥1:8 (Seroprotection)	91.7 (88.7; 94.1) N=433	67.7 (63.1; 72.1) N=431	23.9 (18.8; 29.0)	

Serogroup Endpoint	MenQuadfi (95% CI)	MenACWY-PS (95% CI)	% difference MenQuadfi – MenACWY-PS (95% CI)	MenQuadfi / MenACWY-PS (95% CI)
% Seroresponse§	74.4 (70.0; 78.4) N=433	43.4 (38.7; 48.2) N=431	31.0 (24.6; 37.0)	
hSBA GMT	69.1 (58.7; 81.4) N=433	21.0 (17.4; 25.3) N=431		3.30 (2.57; 4.23)

N: number of participants in per-protocol analysis set with valid serology results
95% CI of the single proportion calculated from the exact binomial method.
95% CI of the difference calculated from the Wilson Score method without continuity correction.
§The overall non-inferiority would be demonstrated if the lower limit of the 2-sided 95% CI is > -10% for all four serogroups.

Booster response

Study MET56 compared the immunogenicity of a booster dose of MenQuadfi to a booster dose of MenACWY-DT in participants at least 15 years of age and primed with quadrivalent meningococcal conjugate vaccine (MCV4; MenACWY-CRM or MenACWY-DT) 4 to 10 years earlier.

At baseline, hSBA seroprotection and GMT were similar for serogroups A, C, W, and Y.

The hSBA seroresponse following a booster dose of MenQuadfi was non-inferior to that following a booster dose of MenACWY-DT for all four serogroups.

The percentages of participants with hSBA titres ≥ 1:8 increased from baseline for all serogroups and in both groups. The percentages were comparable in MenQuadfi and MenACWY-DT for all serogroups (see Table 13).

Table 13 - Comparison of Bactericidal Antibody Responses to MenQuadfi and MenACWY-DT 30 Days after Booster Vaccination (MET56)

Serogroup Endpoint	MenQuadfi (95% CI)	MenACWY-DT (95% CI)	%difference MenQuadfi - MenACWY-DT (95% CI)	MenQuadfi / MenACWY-DT (95% CI)
A				
% ≥1:8 (Seroprotection)	100.0 (99.0; 100.0) N=384	99.0 (97.4; 99.7) N=389	1.0 (-0.1; 2.6)	
% Seroresponse§	92.2 (89.0; 94.7) N=384	87.1 (83.4; 90.3) N=389	5.0 (0.735; 9.38)	
hSBA GMT	497 (436; 568) N=384	296 (256; 343) N=389		1.68 (1.38; 2.05)

Serogroup Endpoint	MenQuadfi (95% CI)	MenACWY-DT (95% CI)	%difference MenQuadfi - MenACWY-DT (95% CI)	MenQuadfi / MenACWY-DT (95% CI)
C				
% ≥1:8 (Seroprotection)	99.5 (98.1; 99.9) N=384	99.0 (97.4; 99.7) N=389	0.5 (-1.0; 2.1)	
% Seroresponse§	97.1 (94.9; 98.6) N=384	91.8 (88.6; 94.3) N=389	5.4 (2.16; 8.76)	
hSBA GMT	2,618 (2,227; 3,078) N=384	599 (504; 711) N=389		4.37 (3.45; 5.53)
W				
% ≥1:8 (Seroprotection)	100.0 (99.0; 100.0) N=384	99.7 (98.6; 100.0) N=389	0.3 (-0.8; 1.4)	
% Seroresponse§	98.2 (96.3; 99.3) N=384	90.7 (87.4; 93.4) N=389	7.4 (4.30; 10.9)	
hSBA GMT	1,747 (1,508; 2,025) N=384	723 (614; 853) N=389		2.42 (1.94; 3.01)
Y				
% ≥1:8 (Seroprotection)	99.7 (98.6; 100.0) N=384	99.5 (98.2; 99.9) N=389	0.3 (-1.0; 1.6)	
% Seroresponse§	97.4 (95.3; 98.7) N=384	95.6 (93.1; 97.4) N=389	1.8 (-0.907; 4.55)	
hSBA GMT	2,070 (1,807; 2,371) N=384	811 (699; 941) N=389		2.55 (2.09; 3.12)

N: number of participants in per-protocol analysis set with valid serology results
95% CI of the single proportion calculated from the exact binomial method.
95% CI of the difference calculated from the Wilson Score method without continuity correction.
§The overall non-inferiority would be demonstrated if the lower limit of the 2-sided 95% CI is > -10% for all four serogroups

Clinical data are not available after booster vaccination in subjects primed with MenQuadfi.

Concomitantly Administered Vaccines

A Phase III study MET57 was performed in meningococcal vaccine naive toddlers to evaluate the efficacy of MenQuadfi concomitantly administered with MMR, V, PCV13, and DTPa-IPV-HB-Hib and showed no clinically relevant interference on antibody responses to each of the antigens. Overall, the immunogenicity profile of MenQuadfi administered alone was comparable to the MenQuadfi administered concomitantly with licensed paediatric vaccines (MMR+V, DTPa-IPV-HB-Hib, or PCV13).

Overall, the immunogenicity profile of licensed paediatric vaccines (MMR+V, DTPa-IPV-HB-Hib, or PCV13) administered alone without MenQuadfi was comparable to that of the licensed paediatric vaccines administered concomitantly with MenQuadfi.

A Phase II Study (MET50) was performed in meningococcal naive children and adolescents to evaluate the efficacy of MenQuadfi administered concomitantly with dTpa and HPV vaccines.

The antibody responses to MenQuadfi and to HPV, tetanus and diphtheria antigens were similar in both study groups. The anti-pertussis responses of the dTpa administered concomitantly with MenQuadfi and HPV versus dTpa administered concomitantly with HPV only were non-inferior for the PT antigen and did not meet non-inferiority for the FHA, PRN, FIM antigens. Vaccine response rates were robust and comparable across both groups. This trend is in line with the data available with the existing quadrivalent meningococcal conjugate vaccines. Because there are no established serological correlates of protection for pertussis, the clinical implications of the observed pertussis antigen responses are unknown.

5.2 PHARMACOKINETIC PROPERTIES

No pharmacokinetic studies have been performed.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

MenQuadfi has not been evaluated for genotoxic potential.

Carcinogenicity

MenQuadfi has not been evaluated for carcinogenic potential.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Sodium chloride, sodium acetate and water for injections

6.2 INCOMPATIBILITIES

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 SHELF LIFE

36 months when stored at 2°C to 8°C.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store at 2°C to 8°C (Refrigerate. Do not freeze).

6.5 NATURE AND CONTENTS OF CONTAINER

Pack of 1 or 5 single dose (0.5 mL) vials.

Vial stopper is not made with natural latex.

Not all pack sizes may be marketed.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

After use, any remaining vaccine and container must be disposed of safely, according to locally acceptable procedures.

7 MEDICINE SCHEDULE (POISONS STANDARD)

S4 Prescription Only Medicine

8 SPONSOR

Australia:

sanofi-aventis australia pty ltd
Talavera Corporate Centre – Building D
12-24 Talavera Road
Macquarie Park NSW 2113
Australia

Tel: 1800 818 806

New Zealand:

sanofi-aventis new zealand pty ltd
Level 8
56 Cawley St
Ellerslie
Auckland
New Zealand

Tel: 0800 283 684

9 DATE OF FIRST APPROVAL

29 October 2020

10 DATE OF REVISION

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information