

MenQuadfi™

Meningococcal Group A, C, W and Y conjugate vaccine Solution for injection

sanofi

QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose (0.5 mL) contains:

<i>Neisseria meningitidis</i> group A polysaccharide ¹	10 micrograms
<i>Neisseria meningitidis</i> group C polysaccharide ¹	10 micrograms
<i>Neisseria meningitidis</i> group Y polysaccharide ¹	10 micrograms
<i>Neisseria meningitidis</i> group W polysaccharide ¹	10 micrograms

¹Conjugated to tetanus toxoid carrier protein 55 micrograms

For the full list of excipients, see section “*list of excipients.*”

PHARMACEUTICAL FORM

Solution for injection. Clear colourless solution.

CLINICAL PARTICULARS

Therapeutic indications

MenQuadfi is indicated for active immunisation of individuals from the age of 12 months and older against invasive meningococcal disease caused by *Neisseria meningitidis* serogroups A, C, Y and W-135 who travel to or reside in areas with high endemic rates of meningococcal disease or who are at high risk of exposure to *Neisseria meningitidis* serogroups A, C, Y, and W-135.

Posology and method of administration

Posology

Primary vaccination:

- Individuals 12 months of age and older: One single dose (0.5 mL).

Booster vaccination:

- There are no data available to indicate the need for or timing of a booster dose of MenQuadfi (see section “Pharmacodynamic properties”).

Other paediatric population

The safety and immunogenicity of MenQuadfi in individuals under 12 months of age have not yet been established.

Method of administration

For intramuscular injection only, preferably in the deltoid region or anterolateral thigh depending on the recipient's age

and muscle mass.

For instructions on handling of the vaccine before administration, see section “*Special precautions for disposal and other handling*”.

Contraindications

Hypersensitivity to the active substances or to any of the excipients listed in section “*Pharmacodynamic properties*” or after previous administration of the vaccine or a vaccine containing the same components.

Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

MenQuadfi should not be administered subcutaneously, intravascularly or intradermally.

It is good clinical practice to precede vaccination by a review of the medical history (especially with regard to previous vaccination and possible occurrence of undesirable effects) and a clinical examination.

Hypersensitivity

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following administration of the vaccine.

Intercurrent illness

Vaccination should be postponed in individuals suffering from an acute severe febrile illness. However, the presence of a minor infection, such as cold, should not result in the deferral of vaccination.

Syncope

Syncope (fainting) and other anxiety-related reactions can occur following or even before any vaccination as a psychogenic response to the needle injection. Procedures should be in place to prevent falling or injury and to manage syncope.

Thrombocytopenia and coagulation disorders

MenQuadfi should be given with caution to individuals with thrombocytopenia or any coagulation disorder that would contraindicate intramuscular injection, unless the potential benefit clearly outweighs the risk of administration.

Protection

MenQuadfi will only protect against *Neisseria meningitidis* groups A, C, W, and Y. The vaccine will not protect against any other *Neisseria meningitidis* groups.

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

Waning of serum bactericidal antibody titres against serogroup A when using human complement in the assay (hSBA) has been reported for MenQuadfi and other quadrivalent meningococcal vaccines. The clinical relevance of this observation is unknown. 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.

Lower hSBA geometric mean titers (GMTs) against serogroup A have been observed after a single dose of MenQuadfi was administered to toddlers who previously received serogroup C meningococcal conjugate vaccine (MenC-CRM) during infancy. Nevertheless, seroprotection rates were comparable between treatment groups (see section "*Pharmacodynamic properties*"). The clinical relevance of this observation is unknown. This aspect might be considered for individuals at high risk for MenA infection who received MenC-CRM vaccine in their first year of life.

Immunodeficiency

It may be expected that in patients receiving immunosuppressive treatment or patients with immunodeficiency, an adequate immune response may not be elicited (see section "*Interaction with other medicinal products and other forms of interaction*"). Persons with familial complement deficiencies (for example, C5 or C3 deficiencies) and persons receiving treatments that inhibit terminal complement activation (for example, eculizumab) are at increased risk of invasive disease caused by *Neisseria meningitidis* groups A, C, W, and Y, even if they develop antibodies following vaccination with MenQuadfi. No data on immunocompromised patients are available.

Tetanus immunization

Immunization with MenQuadfi vaccine does not substitute for routine tetanus immunization.

Co-administration of MenQuadfi with a tetanus toxoid-containing vaccine does not impair the response to tetanus toxoid or impact the safety.

Sodium content

This medicine contains less than 1 mmol sodium (23 mg) per dose that is to say essentially 'sodium-free'.

Interaction with other medicinal products and other forms of interaction

Use with other vaccines

Injection sites on separate limbs and separate syringes must be used in the case of concomitant administration.

For ages 12-23 months, MenQuadfi can be co-administered with the measles-mumps-rubella vaccine (MMR) and varicella vaccine (V), combined diphtheria - tetanus - acellular pertussis (DTaP) vaccines, including combination DTaP vaccines with hepatitis B (HBV), inactivated poliovirus (IPV) or *Haemophilus influenzae* type b (Hib) such as DTaP-IPV-HB-Hib (Hib conjugated to tetanus toxoid) vaccine and 13-valent pneumococcal polysaccharide conjugated vaccine (PCV-13).

For ages 10-17 years, MenQuadfi can be co-administered with diphtheria, tetanus, pertussis (acellular, component) vaccine (adsorbed, reduced antigen(s) content) (Tdap) and human papillomavirus vaccine (recombinant, adsorbed) (HPV).

There was no impact on the immune response to MenQuadfi when a meningococcal serogroup B vaccine was co-administered.

MenQuadfi can be administered concomitantly with PCV-13. Lower hSBA GMTs on day 30 post-dose for serogroup A has been observed when given concomitantly. The clinical relevance of this observation is unknown. As a precaution in children 12-23 months of age at high risk for serogroup A disease, consideration might be given for administration of MenQuadfi and PCV-13 vaccines separately.

Meningococcal vaccine naïve children aged 10-17 years had non inferior response for PT and lower antibody responses to FHA, PRN and FIM when Tdap vaccine was administered concomitantly with MenQuadfi and HPV compared to co-administration with HPV vaccine alone. The clinical implications of the observed pertussis antigen responses also

observed with the existing quadrivalent meningococcal conjugate vaccines are unknown.

Concomitant vaccines should always be administered at separate injection sites and preferably contralateral.

Concomitant administration of MenQuadfi and other vaccines than those listed above has not been studied.

Use with systemic immunosuppressive medicinal products

It may be expected that in patients receiving immunosuppressive treatment an adequate immune response may not be elicited (see also section “*Special warnings and precautions for use*”).

Fertility, pregnancy, and lactation Pregnancy

There is limited amount of data on the use of MenQuadfi in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section “*Preclinical safety data*”).

Breastfeeding

It is unknown whether MenQuadfi is excreted in human milk.

Fertility

A developmental and reproductive toxicity study was performed in female rabbits. There were no effects on mating performances or female fertility. No study was conducted on male fertility (see section “*Preclinical safety data*”).

Effects on ability to drive and use machines

MenQuadfi has no or negligible influence on the ability to drive and use machines. However, some of the effects mentioned under section 4.8 “Undesirable effects” may temporarily affect the ability to drive or use machines.

Undesirable effects

Summary of the safety profile

The safety of a single dose of MenQuadfi in individuals 12 months of age and older was evaluated in seven randomized, active-controlled, multi-centre pivotal studies. In these studies, 6,308 subjects received either a primary dose (N=5,906) or a booster dose (N=402) of MenQuadfi and were included in the safety analyses. This included 1,389 toddlers aged 12 through 23 months of age, 498 children aged 2 through 9 years, 2,289 adolescents aged 10 through 17 years, 1,684 adults aged 18 through 55 years, 199 older adults aged 56 through 64 years, and 249 elderly aged 65 years and older. Of these, 392 adolescents received MenQuadfi co-administered with Tdap and HPV, and 589 toddlers received MenQuadfi co-administered with MMR+V (N=189), DTaP-IPV-HB-Hib (N=200) or PCV-13 (N=200).

The most frequently reported adverse reactions within 7 days after vaccination with a single dose of MenQuadfi alone in toddlers 12 through 23 months of age were irritability (36.7%) and injection site tenderness (30.6%) and in ages 2 years and above were injection site pain (38.7%) and myalgia (30.5%). These adverse reactions were mostly mild or moderate in intensity.

Rates of adverse reactions after a booster dose of MenQuadfi in adolescents and adults at least 15 years of age were comparable to those seen in adolescents and adults who received a primary dose of MenQuadfi.

Rates of adverse reactions within 7 days following vaccination among toddlers were comparable when MMR+V were given concomitantly with or without MenQuadfi, and when DTaP-IPV-HB-Hib was given with or without MenQuadfi.

Overall, the rates of adverse reactions were higher in toddlers who received PCV-13 given concomitantly with MenQuadfi (36.5%) than in toddlers who received PCV-13 alone (17.2%).

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%).

Tabulated list of adverse reactions

The following adverse reactions, as listed below, have been identified from clinical studies conducted with MenQuadfi when given alone to subjects 2 years of age and older. The safety profile observed in toddlers aged 12 through 23 months is presented in the paediatric population section.

The adverse reactions are listed according to the following frequency categories:

Very common ($\geq 1/10$); Common ($\geq 1/100$ to $< 1/10$);

Uncommon ($\geq 1/1,000$ to $< 1/100$); Rare ($\geq 1/10,000$ to $< 1/1,000$).

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 1: Tabulated summary of adverse reactions following administration of MenQuadfi from clinical trials in subjects 2 years of age and above

MedDRA System Organ Class	Frequency	Adverse reactions
Blood and lymphatic system disorders	Rare	Lymphadenopathy
Nervous system disorders	Very common	Headache
	Uncommon	Dizziness
Gastrointestinal disorders	Uncommon	Vomiting, nausea
	Rare	Diarrhoea, stomach pain
Skin and subcutaneous tissue disorders	Rare	Urticaria, pruritus, rash
Musculoskeletal and connective tissue disorders	Very common	Myalgia
	Rare	Pain in extremity
General disorders and administration site conditions	Very common	Malaise
		Injection site pain
	Common	Fever
		At the injection site: swelling, erythema
	Uncommon	Fatigue
		At the injection site: pruritus, warmth, bruising, rash
	Rare	Chills, axillary pain
		At the injection site: induration

Paediatric population

The safety profile of MenQuadfi in children and adolescents 2 through 17 years of age was generally comparable to that in adults. Injection site erythema and swelling at the MenQuadfi injection site were reported more frequently in children 2 through 9 years of age (very common) than in the older age groups.

In toddlers 12 through 23 months of age, injection site erythema and swelling (very common) at the MenQuadfi injection site, vomiting (common) and diarrhoea (common), were reported more frequently than in the older age groups. The following additional reactions, as listed below in Table 2, have been reported very commonly or commonly following administration of MenQuadfi in toddlers during clinical trials:

Table 2: Tabulated summary of adverse reactions following administration of MenQuadfi from clinical trials in subjects 12 months through 23 months

MedDRA System Organ Class	Frequency	Adverse reactions
Metabolic and nutrition disorders	Very common	Appetite lost
Psychiatric disorders	Very common	Irritability
	Uncommon	Insomnia
Nervous system disorders	Very common	Drowsiness
Gastrointestinal disorders	Common	Vomiting, diarrhoea
Skin and subcutaneous tissue disorders	Uncommon	Urticaria
General disorders and administration site conditions	Very Common	Abnormal crying
		At the injection site: tenderness/pain, erythema, swelling
	Common	Fever
	Uncommon	At the injection site: pruritus, induration, bruising, rash

Older population

Overall, within 7 days after vaccination with a single dose of MenQuadfi, the same injection site and systemic adverse reactions were observed in older (≥ 56 years of age) and younger adults (18 through 55 years old) but at lower frequencies; except for injection site pruritus, which was more frequent (common) in older adults. These adverse reactions mostly were mild or moderate in intensity.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation 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 reaction via farmakovigilans@kalventis.com

and Pusat Farmakovigilans/MESO Nasional Direktorat Pengawasan Keamanan, Mutu, dan Ekspor Impor Obat, Narkotika, Psikotropika, Prekursor dan Zat Adiktif Badan Pengawas Obat dan Makanan. Jl. Percetakan Negara No. 23, Jakarta Pusat, 10560

Email: pv-center@pom.go.id

Phone: +62-21-4244691 Ext.1079

Website: <https://e-meso.pom.go.id/>.

Overdose

Overdose with MenQuadfi is unlikely due to its presentation as a single dose vial. In the event of overdose, monitoring of vital functions and possible symptomatic treatment is recommended

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Pharmacotherapeutic group:
meningococcal vaccines **ATC code:**
J07AH08

Mechanism of action

Anti-capsular meningococcal antibodies protect against meningococcal diseases via complement mediated bactericidal activity.

MenQuadfi induces the production of bactericidal antibodies specific to the capsular polysaccharides of *Neisseria meningitidis* serogroups A, C, W, and Y.

Immunogenicity

The immunogenicity 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 six pivotal studies and in one additional study in toddlers (12-23 months of age). The immunogenicity of a single dose of MenQuadfi for booster vaccination (subjects 15 to 55 years of age) was assessed in one pivotal study. In addition, 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).

Primary immunogenicity analyses were conducted by measuring serum bactericidal activity (SBA) using human serum as the source of exogenous complement (hSBA). Rabbit complement (rSBA) data are available in subsets in all age groups and generally follows the trends observed with human complement (hSBA) data. In addition, all subjects were assessed for primary immunogenicity measured by hSBA and rSBA for serogroup C in MEQ00065 study [NCT03890367].

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.

Immunogenicity in Toddlers 12 to 23 month of age

Immunogenicity in subjects 12 through 23 months of age was evaluated in three clinical studies (MET51 [NCT02955797], MET57 [NCT03205371] and MEQ00065 [NCT03890367]).

MET51 was conducted in subjects who were either meningococcal vaccine naïve or had been primed with monovalent meningococcal C conjugate vaccines in their first year of life (see table 3).

Table 3: Comparison of bactericidal antibody responses to MenQuadfi and MenACWY-TT vaccine 30 days after vaccination of meningococcal vaccine naïve subjects only or combined (naïve + MenC primed) subjects 12 through 23 months of age (study MET51*)

Endpoint by Serogroup	MenQuadfi (95% CI) Naïve	MenACWY-TT (95% CI) Naïve	MenQuadfi (95% CI) Combined (Naïve + MenC Primed)	MenACWY-TT (95% CI) Combined (Naïve + MenC Primed)
A	N=293	N=295	N=490	N=393-394
% $\geq 1:8$ (Seroprotection)**	90.8 (86.9; 93.8)	89.5 (85.4; 92.7)	90.4 (87.4; 92.9)	91.6 (88.4; 94.2)
% Seroreponse	76.8 (71.5; 81.5)	72.5 (67.1; 77.6)	76.5 (72.5; 80.2)	77.1 (72.6; 81.2)
hSBA GMT	28.7	28.0	29.9	34.5

	(25.2; 32.6)	(24.4; 32.1)	(26.9; 33.2)	(30.5; 39.0)
C	N=293	N=295	N=489	N=393-394
% ≥1:8 (Seroprotection)**	99.3 (97.6; 99.9)	81.4 (76.4; 85.6)	99.2 (97.9; 99.8)	85.5 (81.7; 88.9)
% Seroresponse	98.3 (96.1; 99.4)	71.5 (66.0; 76.6)	97.1 (95.2; 98.4)	77.4 (72.9; 81.4)
hSBA GMT	436 (380; 500)	26.4 (22.5; 31.0)	880 (748; 1035)	77.1 (60.7; 98.0)
W	N=293	N=296	N=489	N=393-394
% ≥1:8 (Seroprotection)**	83.6 (78.9; 87.7)	83.4 (78.7; 87.5)	84.9 (81.4; 87.9)	84.0 (80.0; 87.5)
% Seroresponse	67.6 (61.9; 72.9)	66.6 (60.9; 71.9)	70.8 (66.5; 74.8)	68.4 (63.6; 73.0)
hSBA GMT	22.0 (18.9; 25.5)	16.4 (14.4; 18.6)	24.4 (21.8; 27.5)	17.7 (15.8; 19.8)
Y	N=293	N=296	N=488-490	N=394-395
% ≥1:8 (Seroprotection)**	93.2 (89.7; 95.8)	91.6 (87.8; 94.5)	94.3 (91.8; 96.2)	91.6 (88.5; 94.2)
% Seroresponse	81.9 (77.0; 86.1)	79.1 (74.0; 83.5)	84.8 (81.3; 87.9)	78.9 (74.6; 82.9)
hSBA GMT	38.0 (33.0; 43.9)	32.2 (28.0; 37.0)	41.7 (37.5; 46.5)	31.9 (28.4; 36.0)

* Clinical trial identifier NCT02955797

N: number of subjects in the per-protocol analysis set with valid serology results. The number of participants varies depending on the timepoints and serogroup.
95% CI of the single proportion calculated from the exact binomial method.

** Non-inferiority criterion met

Response in subjects previously vaccinated with MenC conjugate vaccines in their first year of life:

The majority of monovalent meningococcal C conjugate vaccine primed toddlers (12-23 months of age) in study MET51 (NCT02955797) had hSBA titres ≥1:8 in the MenQuadfi group (N=198) (≥ 86.7%) and in MenACWY-TT group (N=99) (≥ 85.7%) at D30 post-vaccination. These toddlers received during their infancy MenC-TT or MenC-CRM vaccines. Post- vaccination seroprotection rates were comparable between MenQuadfi and MenACWY-TT for all serogroups regardless of the priming background.

In MenC-CRM primed subjects the GMTs for serogroup A were lower in the MenQuadfi group (n=49) than in the MenACWY- TT group (n=25) [12.0 (8.23; 17.5) vs 42.2 (25.9; 68.8)]. After administration of MenQuadfi seroprotection rates (hSBA titres ≥1:8) for subjects primed with MenC-CRM were lower but still comparable for serogroups A and W compared with those in the MenACWY-TT group [A: 68.8% (53.7; 81.3) vs 96.0% (79.6; 99.9)]; W: 68.1% (52.9; 80.9) vs 79.2% (57.8; 92.9)]. The rates for serogroup Y were higher but still comparable with those in the MenACWY-TT group [95.8% (85.7 ; 99.5) vs 80.0% (59.3; 93.2)]. The rates for serogroup C were comparable in both groups [95.7% (85.5; 99.5) vs 92.0% (74.0; 99.0)]. The clinical relevance of these results is unknown. This aspect might/ be considered for individuals at high risk for MenA infection who received MenC-CRM vaccine in their first year of life.

MET57 (NCT03205371) was conducted in meningococcal vaccine naïve toddlers 12 through 23 months of age to assess the immunogenicity of the concomitant administration of MenQuadfi with paediatric vaccines (MMR+V, DTaP-IPV-HB-Hib or PCV-13). Overall, the post-vaccination hSBA seroprotection rates in subjects who received MenQuadfi was high for all serogroups (between 88.9% and 100%). Seroresponse and seroprotection rates for serogroup A were comparable when MenQuadfi was co-administered with PCV-13 and alone (56.1%, [95% CI 48.9; 63.2] and 83.7% [95% CI 77.7; 88.6] vs 71.9% [95%CI 61.8; 80.6] and 90.6% [95%CI 82.9; 95.6]). There were differences in the hSBA GMTs for serogroup A when MenQuadfi was co-administered with PCV-13 (n=196) compared with MenQuadfi administered alone (n=96) (24.6 [95%CI 20.2; 30.1] and 49.0 [95%CI 36.8; 65.3]). The clinical relevance of these

results are unknown but this observation might be taken into consideration for individuals at high risk for MenA infection and consequently vaccinations with MenQuadfi and PCV13 might be performed separately.

MEQ00065 (NCT03890367) study was conducted in meningococcal vaccine naïve toddlers 12 through 23 months of age to assess the immunogenicity of serogroup C using hSBA and rSBA assays following administration of a single dose of MenQuadfi compared to MenACWY-TT or to MenC-TT.

Superiority of MenQuadfi was demonstrated in comparison to MenACWY-TT vaccine for the hSBA seroprotection rate and hSBA and rSBA GMTs to meningococcal serogroup C. Non-inferiority was demonstrated for the rSBA seroprotection rate to meningococcal serogroup C.

Superiority of MenQuadfi was also demonstrated in comparison to MenC-TT vaccine for the rSBA and hSBA GMTs to meningococcal serogroup C and non-inferiority was demonstrated for the rSBA and hSBA seroprotection rates to meningococcal serogroup C (see table 4).

Table 4: Comparison of hSBA and rSBA bactericidal antibody responses for serogroup C to MenQuadfi, MenACWY-TT and MenC-TT vaccines 30 days after vaccination of meningococcal vaccine naïve subjects 12 through 23 months of age (study MEQ00065*)

Endpoints	MenQuadfi (95% CI)	MenACWY-TT (95% CI)	MenC-TT (95% CI)	MenQuadfi (95% CI)	MenACWY-TT (95% CI)	MenC-TT (95% CI)
	hSBA			rSBA		
	N=214	N=211	N= 216	N=213	N=210	N= 215
% ≥1:8 (Seroprotection)	99.5 [#] § (97.4; 100)	89.1 (84.1; 93.0)	99.5 (97.4; 100)	100 [¶] (98.3; 100)	94.8 (90.8; 97.4)	100 (98.3; 100)
% Seroreponse	99.5 (97.4; 100)	83.4 (77.7; 88.2)	99.1 (96.7; 99.9)	99.5 (97.4; 100)	92.9 (88.5; 95.9)	99.5 (97.4; 100)
GMTs	515 [§] (450; 591)	31,6 (26.5; 37.6)	227 (198; 260)	2143 [¶] (1870; 2456)	315 (252; 395)	1624 (1425; 1850)

* Clinical trial identifier NCT03890367

[#] superiority of MenQuadfi demonstrated versus MenACWY-TT (hSBA seroprotection rates)

[§] non inferiority of MenQuadfi demonstrated versus MenC-TT (hSBA seroprotection rates)

[§] superiority of MenQuadfi demonstrated versus MenACWY-TT and MenC-TT (hSBA GMTs)

[¶] non inferiority of MenQuadfi demonstrated versus MenACWY-TT and MenC-TT (rSBA seroprotection rates)

[¶] superiority of MenQuadfi demonstrated versus MenACWY-TT and MenC-TT (rSBA GMTs)

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

Immunogenicity in Children 2 through 9 years of age

Immunogenicity in subjects 2 through 9 years of age was evaluated in study MET35 (NCT03077438) (stratified by ages 2 through 5 and 6 through 9 years) comparing seroresponses following administration of either MenQuadfi or MenACWY-CRM.

Overall, for subjects 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.

Table 5: Comparison of bactericidal antibody responses to MenQuadfi and MenACWY-CRM 30 days after vaccination in meningococcal vaccine naïve subjects 2 through 5 years and 6 through 9 years of age (study MET35*)

2-5 years			6-9 years	
Endpoint by Serogroup	MenQuadfi (95% CI)	MenACWY-CRM (95% CI)	MenQuadfi (95% CI)	MenACWY-CRM (95% CI)
A	N=227-228	N=221	N=228	N=237
% ≥1:8 (Seroprotection)	84.6 (79.3; 89.1)	76.5 (70.3; 81.9)	88.2 (83.2; 92.0)	81.9 (76.3; 86.5)
% Seroresponse	52.4 (45.7; 59.1)	44.8 (38.1; 51.6)	58.3 (51.6; 64.8)	50.6 (44.1; 57.2)
hSBA GMT	21.6 (18.2; 25.5)	18.9 (15.5; 23.0)	28.4 (23.9; 33.8)	26.8 (22.0; 32.6)
C	N=229	N=222-223	N=229	N=236
% ≥1:8 (Seroprotection)	97.4 (94.4; 99.0)	64.6 (57.9; 70.8)	98.3 (95.6; 99.5)	69.5 (63.2; 75.3)
% Seroresponse	94.3 (90.5; 96.9)	43.2 (36.6; 50.0)	96.1 (92.7; 98.2)	52.1 (45.5; 58.6)
hSBA GMT	208 (175; 246)	11.9 (9.79; 14.6)	272 (224; 330)	23.7 (18.2; 31.0)
W	N=229	N=222	N=229	N=237
% ≥1:8 (Seroprotection)	90.8 (86.3; 94.2)	80.6 (74.8; 85.6)	98.7 (96.2; 99.7)	91.6 (87.3; 94.8)
% Seroresponse	73.8 (67.6; 79.4)	61.3 (54.5; 67.7)	83.8 (78.4; 88.4)	66.7 (60.3; 72.6)
hSBA GMT	28.8 (24.6; 33.7)	20.1 (16.7; 24.2)	48.9 (42.5; 56.3)	33.6 (28.2; 40.1)
Y	N=229	N=222	N=229	N=237
% ≥1:8 (Seroprotection)	97.8 (95.0; 99.3)	86.9 (81.8; 91.1)	99.1 (96.9; 99.9)	94.5 (90.8; 97.0)
% Seroresponse	88.2 (83.3; 92.1)	77.0 (70.9; 82.4)	94.8 (91.0; 97.3)	81.4 (75.9; 86.2)
hSBA GMT	49.8 (43.0; 57.6)	36.1 (29.2; 44.7)	95.1 (80.2; 113)	51.8 (42.5; 63.2)

* Clinical trial identifier NCT03077438

N: number of subjects in the per-protocol analysis set with valid serology results. The number of participants varies depending on the timepoints and serogroup.
95% CI of the single proportion calculated from the exact binomial method.

Immunogenicity in Children and adolescents 10 through 17 years of age

Immunogenicity in subjects aged 10 through 17 years of age was evaluated in two studies comparing seroresponses following administration of MenQuadfi compared to either MenACWY-CRM (MET50 [NCT02199691]) or MenACWY-DT (MET43[NCT02842853]).

MET50 was conducted in meningococcal vaccine naïve subjects and seroresponse was evaluated following administration with either MenQuadfi alone, MenACWY-CRM alone, MenQuadfi co-administered with Tdap and HPV or Tdap and HPV alone.

Table 6: Comparison of bactericidal antibody responses to MenQuadfi and MenACWY-CRM 30 days after vaccination in meningococcal vaccine naïve subjects 10 through 17 years of age (study MET50*)

Endpoint by Serogroup	MenQuadfi (95% CI)		MenACWY-CRM (95% CI)	
A	N=463		N=464	
% ≥1:8 (Seroprotection)	93.5	(90.9; 95.6)	82.8	(79.0; 86.1)
% Seroresponse**	75.6	(71.4; 79.4)	66.4	(61.9; 70.7)
hSBA GMT	44.1	(39.2; 49.6)	35.2	(30.3; 41.0)
C	N=462		N=463	
% ≥1:8 (Seroprotection)	98.5	(96.9; 99.4)	76.0	(71.9; 79.8)
% Seroresponse**	97.2	(95.2; 98.5)	72.6	(68.3; 76.6)
hSBA GMT	387	(329; 456)	51.4	(41.2; 64.2)
W	N=463		N=464	
% ≥1:8 (Seroprotection)	99.1	(97.8; 99.8)	90.7	(87.7; 93.2)
% Seroresponse**	86.2	(82.7; 89.2)	66.6	(62.1; 70.9)
hSBA GMT	86.9	(77.8; 97.0)	36.0	(31.5; 41.0)
Y	N=463		N=464	
% ≥1:8 (Seroprotection)	97.2	(95.2; 98.5)	83.2	(79.5; 86.5)
% Seroresponse**	97.0	(95.0; 98.3)	80.8	(76.9; 84.3)
hSBA GMT	75.7	(66.2; 86.5)	27.6	(23.8; 32.1)

* Clinical trial identifier NCT02199691

N: number of subjects in the per-protocol analysis set with valid serology results.

95% CI of the single proportion calculated from the exact binomial method.

** Post-vaccination hSBA titres ≥1:8 for subjects with pre-vaccination hSBA titres < 1:8 or at least a 4-fold increase in hSBA titres from pre to post-vaccination for subjects with pre-vaccination hSBA titres ≥1:8

Non-inferiority criterion met.

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

Table 7: Comparison of bactericidal antibody responses to MenQuadfi and MenACWY-DT 30 days after vaccination in meningococcal vaccine naïve subjects 10 through 17 years of age (study MET43*)

Endpoint by Serogroup	MenQuadfi (95% CI)		MenACWY-DT (95% CI)	
A	N=1,097		N=300	
% ≥1:8 (Seroprotection)	96.2	(94.9; 97.2)	89.0	(84.9; 92.3)
% Seroresponse**	74.0	(71.3; 76.6)	55.3	(49.5; 61.0)
hSBA GMT	78	(71.4; 85.2)	44.2	(36.4; 53.7)
C	N=1,097-1,098		N=300	
% ≥1:8 (Seroprotection)	98.5	(97.5; 99.1)	74.7	(69.3; 79.5)

% Seroreponse**	95.6	(94.2; 96.8)	53.3	(47.5; 59.1)
hSBA GMT	504	(456; 558)	44.1	(33.7; 57.8)
W	N=1,097		N=300	
% ≥1:8 (Seroprotection)	98.3	(97.3; 99.0)	93.7	(90.3; 96.1)
% Seroreponse**	84.5	(82.2; 86.6)	72.0	(66.6; 77.0)
hSBA GMT	97.2	(88.3; 107)	59.2	(49.1; 71.3)
Y	N=1,097		N=300	
% ≥1:8 (Seroprotection)	99.1	(98.3; 99.6)	94.3	(91.1; 96.7)
% Seroreponse**	95.6	(94.2; 96.8)	85.7	(81.2; 89.4)
hSBA GMT	208	(189; 228)	80.3	(65.6; 98.2)

* Clinical trial identifier NCT02842853

N: number of subjects in the per-protocol analysis set with valid serology results. The number of participants varies depending on the timepoints and serogroup.

95% CI of the single proportion calculated from the exact binomial method.

** Non-inferiority criterion met.

Immunogenicity in Adults 18 through 55 years of age

Immunogenicity in subjects from 18 through 55 years of age was evaluated in study MET43 (NCT02842853) comparing MenQuadfi to MenACWY-DT.

Table 8: Comparison of bactericidal antibody responses to MenQuadfi and MenACWY-DT 30 days after vaccination in meningococcal vaccine naïve subjects 18 through 55 years of age (study MET43*)

Endpoint by Serogroup	MenQuadfi (95% CI)		MenACWY-DT (95% CI)	
A	N=1,406-1,408		N=293	
% ≥1:8 (Seroprotection)	93.5	(92.1; 94.8)	88.1	(83.8; 91.5)
% Seroreponse**	73.5	(71.2; 75.8)	53.9	(48.0; 59.7)
hSBA GMT	106	(97.2; 117)	52.3	(42.8; 63.9)
C	N=1,406-1,408		N=293	
% ≥1:8 (Seroprotection)	93.5	(92.0; 94.7)	77.8	(72.6; 82.4)
% Seroreponse**	83.4	(81.4; 85.3)	42.3	(36.6; 48.2)
hSBA GMT	234	(210; 261)	37.5	(29.0; 48.5)
W	N=1,408-1,410		N=293	
% ≥1:8 (Seroprotection)	94.5	(93.2; 95.7)	80.2	(75.2; 84.6)
% Seroreponse**	77.0	(74.7; 79.2)	50.2	(44.3; 56.0)
hSBA GMT	75.6	(68.7; 83.2)	33.2	(26.3; 42.0)
Y	N=1,408-1,410		N=293	
% ≥1:8 (Seroprotection)	98.6	(97.8; 99.1)	81.2	(76.3; 85.5)
% Seroreponse**	88.1	(86.3; 89.8)	60.8	(54.9; 66.4)
hSBA GMT	219	(200; 239)	54.6	(42.3; 70.5)

* Clinical trial identifier NCT02842853

N: number of subjects in the per-protocol analysis set with valid serology results. The number of participants varies depending on the timepoints and serogroup.

95% CI of the single proportion calculated from the exact binomial method.

** Non-inferiority criterion met.

Immunogenicity in Adults 56 years of age and older

Immunogenicity in adults ≥ 56 years of age (mean 67.1 years, range 56.0 – 97.2 years) was assessed in study MET49 (NCT02842866) comparing the immunogenicity of MenQuadfi to MenACWY polysaccharide vaccine.

Table 9: Comparison of bactericidal antibody responses to MenQuadfi and MenACWY polysaccharide in meningococcal vaccine naïve in subjects 56 years of age and older 30 days after vaccination (study MET49*)

Endpoint by Serogroup	MenQuadfi (95% CI)	MenACWY polysaccharide (95% CI)
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A	N=433		N=431	
% ≥1:8 (Seroprotection)	89.4	(86.1; 92.1)	84.2	(80.4; 87.5)
% Seroresponse**	58.2	(53.4; 62.9)	42.5	(37.7; 47.3)
hSBA GMT	55.1	(46.8; 65.0)	31.4	(26.9; 36.7)
C	N=433		N=431	
% ≥1:8 (Seroprotection)	90.1	(86.9; 92.7)	71.0	(66.5; 75.2)
% Seroresponse**	77.1	(72.9; 81.0)	49.7	(44.8; 54.5)
hSBA GMT	101	(83.8; 123)	24.7	(20.7; 29.5)
W	N=433		N=431	
% ≥1:8 (Seroprotection)	77.4	(73.1; 81.2)	63.1	(58.4; 67.7)
% Seroresponse**	62.6	(57.8; 67.2)	44.8	(40.0; 49.6)
hSBA GMT	28.1	(23.7; 33.3)	15.5	(13.0; 18.4)
Y	N=433		N=431	
% ≥1:8 (Seroprotection)	91.7	(88.7; 94.1)	67.7	(63.1; 72.1)
% Seroresponse**	74.4	(70.0; 78.4)	43.4	(38.7; 48.2)
hSBA GMT	69.1	(58.7; 81.4)	21.0	(17.4; 25.3)

* Clinical trial identifier NCT02842866

N: number of subjects in the per-protocol analysis set with valid serology results.

95% CI of the single proportion calculated from the exact binomial method.

** Non-inferiority criterion met.

Persistence of immune response and MenQuadfi booster response

Antibody persistence after primary vaccination and immunogenicity of a MenQuadfi 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)

Persistence of immune response and MenQuadfi booster response in children 4 through 5 years of age
MET62 (NCT03476135) evaluated the antibody persistence of a primary dose, immunogenicity and the safety of a booster dose of MenQuadfi in children 4-5 years of age. These children were primed with a single dose of MenQuadfi or MenACWY-TT 3 years before as part of the phase II study MET54 when they were 12-23 months old. The antibody persistence prior to the MenQuadfi booster dose and the booster immune response were assessed according to the vaccine (MenQuadfi or MenACWY-TT) children had received 3 years ago (Table 10).

For all serogroups, hSBA GMTs were higher at D30 post-primary dose than at D0 pre-booster dose for MenQuadfi or MenACWY-TT. The pre-booster GMTs were higher than the pre-primary dose, indicative of long-term persistence of immune response.

After the booster dose, seroprotection rates were nearly 100% for all serogroups in children primed with MenQuadfi.

Table 10: Comparison of bactericidal antibody response 30 days after booster vaccination, and persistence in children (4-5 years) primed with MenQuadfi or MenACWY-TT 3 years before in study MET54* – (study MET62)**

Serogroup Endpoint	MenQuadfi Booster in MenQuadfi primed (95% CI)			MenQuadfi Booster in MenACWY-TT primed (95% CI)			MenQuadfi Booster in MenQuadfi primed + MenACWY-TT primed (95% CI)		
	Persistence# N=42		Booster\$ N=40	Persistence# N=49		Booster\$ N=44	Persistence# N=91		Booster\$ N=84
	D30 Post primary dose	D0-Pre-booster dose		D30 Post primary dose	D0-Pre-booster dose		D30 Post primary dose	D0-Pre-booster dose	

A									
% ≥1:8 (Seroprotection)	97.6 (87.4; 99.9)	66.7 (50.5; 80.4)	100 (91.2; 100)	89.8 (77.8; 96.6)	83.7 (70.3; 92.7)	100 (92.0; 100)	93.4 (86.2; 97.5)	75.8 (65.7; 84.2)	100 (95.7; 100)
% Seroresponse	-	-	100 (91.2; 100)	-	-	95.5 (84.5; 99.4)	-	-	97.6 (91.7; 99.7)
hSBA GMT	83.3 (63.9; 109)	11.9 (8.11; 17.4)	763 (521; 1117)	49.6 (32.1; 76.7)	14.7 (10.7; 20.2)	659 (427; 1017)	63.0 (48.3; 82.2)	13.3 (10.5; 17.0)	706 (531; 940)
C									
% ≥1:8 (Seroprotection)	100 (91.6; 100)	100 (91.6; 100)	100 (91.2; 100)	87.8 (75.2; 95.4)	57.1 (42.2; 71.2)	100 (92.0; 100)	93.4 (86.2; 97.5)	76.9 (66.9; 85.1)	100 (95.7; 100)
% Seroresponse	-	-	95.0 (83.1; 99.4)	-	-	100 (92.0; 100)	-	-	97.6 (91.7; 99.7)
hSBA GMT	594 (445; 793)	103 (71.7; 149)	5894 (4325; 8031)	29.4 (20.1; 43.1)	11.6 (7.28; 18.3)	1592 (1165; 2174)	118 (79.3; 175)	31.8 (21.9; 46.1)	2969 (2293; 3844)
W									
% ≥1:8 (Seroprotection)	100 (91.6; 100)	97.6 (87.4; 99.9)	97.5 (86.8; 99.9)	95.9 (86.0; 99.5)	83.7 (70.3; 92.7)	100 (92.0; 100)	97.8 (92.3; 99.7)	90.1 (82.1; 95.4)	98.8 (93.5; 100)
% Seroresponse	-	-	97.5 (86.8; 99.9)	-	-	100 (92.0; 100)	-	-	98.8 (93.5; 100)
hSBA GMT	71.8 (53.3; 96.7)	50.0 (35.9; 69.5)	2656 (1601; 4406)	40.1 (30.6; 52.6)	21.2 (14.6; 30.9)	3444 (2387; 4970)	52.5 (42.7; 64.5)	31.5 (24.2; 41.0)	3043 (2248; 4120)
Y									
% ≥1:8 (Seroprotection)	100 (91.6; 100)	97.6 (87.4; 99.9)	100 (91.2; 100)	100 (92.7; 100)	89.8 (77.8; 96.6)	100 (92.0; 100)	100 (96.0; 100)	93.4 (86.2; 97.5)	100 (95.7; 100)
% Seroresponse	-	-	100 (91.2; 100)	-	-	100 (92.0; 100)	-	-	100 (95.7; 100)
hSBA GMT	105 (73.9; 149)	32.5 (24.8; 42.7)	2013 (1451; 2792)	75.8 (54.2; 106)	18.2 (13.8; 24.0)	2806 (2066; 3813)	88.1 (69.3; 112)	23.8 (19.4; 29.1)	2396 (1919; 2991)

* Clinical trial identifier MET54 – NCT03205358. The study was conducted in toddlers 12-23 months old.

** Clinical trial identifier MET62 – NCT03476135

\$ N calculated using per protocol analysis set (PPAS) with valid serology results; booster dose = D30 MET62.

N calculated using full analysis set for persistence (FASP) with valid serology results; post-primary dose = D30 MET54, pre-booster dose = D0 MET62.

Vaccine seroresponse: titre is < 1:8 at baseline with post-vaccination titre ≥ 1:16 or titre is ≥ 1:8 at baseline with a ≥ 4-fold increase at post-vaccination.

95% CI of the single proportion calculated from the exact binomial method.

Persistence of immune response and MenQuadfi booster response in adolescents and adults 13 through 26 years of age

MET59 (NCT04084769) evaluated the antibody persistence of primary dose, immunogenicity and safety of a booster dose of MenQuadfi in adolescents and adults 13 through 26 years of age who had received a single dose of MenQuadfi in study MET50 or MET43 or MenACWY-CRM in study MET50 or outside of Sanofi Pasteur trials 3-6 years prior. The antibody persistence prior to the MenQuadfi booster dose and the booster immune response were assessed according to the vaccine (MenQuadfi or MenACWY-CRM) subjects had received 3-6 years previously (see Table 11).

For all serogroups, hSBA GMTs were higher at D30 post-primary dose than at D0 pre-booster for MenQuadfi and

MenACWY-CRM primed subjects. The pre-booster GMTs were higher than the pre-primary dose, indicative of long-term persistence of immune response.

After the booster dose, seroprotection rates were nearly 100% for all serogroups in adolescents and adults primed with MenQuadfi.

Table 11: Comparison of bactericidal antibody response 6 and 30 days after booster vaccination, and persistence in adolescents and adults (13 through 26 years) primed with MenQuadfi or MenACWY-CRM 3-6 years before in study MET50*, MET43 or outside of Sanofi Pasteur trials – (study MET59***)**

Endpoint by Serogroup	MenQuadfi Booster in MenQuadfi primed (95% CI)				MenQuadfi Booster in MenACWY-CRM primed (95% CI)			
	Persistence [^]		Booster [§]		Persistence [^]		Booster [§]	
	D30 – Post primary dose	D0 – Pre-booster dose	D06 – Post booster dose	D30 – Post booster dose	D30 Post primary dose	D0-Pre-booster dose	D06- Post booster dose	D30 – Post booster dose
	N=376	N=379-380	N=46	N=174	N=132-133	N=140	N=45	N=176
A								
% ≥1:8 (Seroprotection)	94.7 (91.9; 96.7)	72.8 (68.0; 77.2)	91.3 (79.2; 97.6)	99.4 (96.8; 100)	81.2 (73.5; 87.5)	71.4 (63.2; 78.7)	95.6 (84.9; 99.5)	99.4 (96.9; 100)
% Seroresponse	-	-	82.6 (68.6; 92.2)	94.8 (90.4; 97.6)	-	-	77.8 (62.9; 88.8)	93.2 (88.4; 96.4)
hSBA GMT	45.2 (39.9; 51.1)	12.5 (11.1; 14.1)	289 (133; 625)	502 (388; 649)	32.8 (25.0; 43.1)	11.6 (9.41; 14.3)	161 (93.0; 280)	399 (318; 502)
C								
% ≥1:8 (Seroprotection)	98.1 (96.2; 99.2)	86.3 (82.4; 89.6)	100 (92.3; 100)	100 (97.9; 100)	74.2 (65.9; 81.5)	49.3 (40.7; 57.9)	97.8 (88.2; 99.9)	100 (97.9; 100)
% Seroresponse	-	-	89.1 (76.4; 96.4)	97.1 (93.4; 99.1)	-	-	93.3 (81.7; 98.6)	98.9 (96.0; 99.9)
hSBA GMT	417 (348; 500)	37.5 (31.6; 44.5)	3799 (2504; 5763)	3708 (3146; 4369)	49.7 (32.4; 76.4)	11.0 (8.09; 14.9)	919 (500; 1690)	2533 (2076; 3091)
W								
% ≥1:8 (Seroprotection)	100 (99.0; 100)	88.9 (85.3; 91.9)	100 (92.3; 100)	100 (97.9; 100)	93.2 (87.5; 96.9)	76.4 (68.5; 83.2)	100 (92.1; 100)	100 (97.9; 100)
% Seroresponse	-	-	97.8 (88.5; 99.9)	97.7 (94.2; 99.4)	-	-	88.9 (75.9; 96.3)	98.9 (96.0; 99.9)
hSBA GMT	82.7 (73.6; 92.9)	28.8 (25.1; 33.0)	1928 (1187; 3131)	2290 (1934; 2711)	45.1 (34.3; 59.4)	14.9 (11.9; 18.6)	708 (463; 1082)	2574 (2178; 3041)
Y								
% ≥1:8 (Seroprotection)	97.9 (95.9; 99.1)	81.8 (77.5; 85.5)	97.8 (88.5; 99.9)	100 (97.9; 100)	88.7 (82.1; 93.5)	52.1 (43.5; 60.7)	100 (92.1; 100)	100 (97.9; 100)
% Seroresponse	-	-	95.7 (85.2; 99.5)	98.9 (95.9; 99.9)	-	-	91.1 (78.8; 97.5)	100 (97.9; 100)
hSBA GMT	91.0 (78.6; 105)	21.8 (18.8; 25.1)	1658 (973; 2826)	2308 (1925; 2767)	36.1 (27.2; 47.8)	8.49 (6.50; 11.1)	800 (467; 1371)	3036 (2547; 3620)

*MET50 – The study was conducted in adolescents (10-17 years of age).

**MET43 – The study was conducted in children, adolescents and adults (10-55 years of age).

***MET59 – NCT04084769

\$N calculated using per protocol analysis set (PPAS 1 and 2) with valid serology results; post-booster dose = D06 or D30 of MET59

[^]N calculated using full analysis set for persistence (FASP) with valid serology results. The number of participants varies depending on the timepoints and serogroup; post-primary dose = D30 MET50 or MET43, pre-booster dose = D0 MET59.

Vaccine seroresponse: titre is <1:8 at baseline with post-vaccination titre $\geq 1:16$ or titre is $\geq 1:8$ at baseline with a ≥ 4 -fold increase at post-vaccination.
95% CI of the single proportion calculated from the exact binomial method.

Persistence of immune response and MenQuadfi booster response in adults 59 years of age and older
MEQ00066 (NCT04142242) evaluated the antibody persistence of primary dose, immunogenicity, and safety of a booster dose of MenQuadfi in adults ≥ 59 years of age who had received a single dose of MenQuadfi or MenACWY-PS ≥ 3 years previously in study MET49 or MET44.

3 year persistence

The antibody persistence prior to the MenQuadfi booster dose and the booster immune response were assessed according to the vaccine (MenQuadfi or MenACWY-PS) subjects had received 3 years previously in MET49 (Table 12).

For all serogroups, hSBA GMTs were higher at D30 post-primary dose than at D0 pre-booster dose for both MenQuadfi-primed and MenACWY-PS-primed adults. In addition, for both primed groups, the pre-booster GMTs were higher than the pre-primary dose for serogroups C, W and Y (indicative of long-term persistence of immune response for these serogroups) and were comparable for serogroup A.

Table 12: Comparison of bactericidal antibody response 6 and 30 days after booster vaccination, and persistence in adults (≥ 59 years) primed with MenQuadfi or MenACWY-PS 3 years before in study MET49* – (study MEQ00066#)

Endpoint by Serogroup	MenQuadfi Booster in MenQuadfi primed (95% CI)				MenQuadfi Booster in MenACWY-PS primed (95% CI)			
	Persistence ^a		Booster ^b		Persistence ^a		Booster ^b	
	D30 - Post primary dose N=212	D0 - Pre-booster dose N=214	D06 - Post booster dose N=58	D30 - Post booster dose N=145	D30 Post primary dose N=168	D0-Pre-booster dose N=169	D06 - Post booster dose N=62	D30 - Post booster dose N=129-130
A								
% $\geq 1:8$ (Seroprotection)	89.6 (84.7; 93.4)	65.0 (58.2; 71.3)	91.4 (81.0; 97.1)	93.8 (88.5; 97.1)	85.7 (79.5; 90.6)	65.7 (58.0; 72.8)	72.6 (59.8; 83.1)	87.7 (80.8; 92.8)
% Seroresponse	-	-	36.2 (24.0; 49.9)	79.3 (71.8; 85.6)	-	-	8.1 (2.7; 17.8)	60.8 (51.8; 69.2)
hSBA GMT	48.9 (39.0; 61.5)	12.2 (10.2; 14.6)	43.7 (26.5; 71.9)	162 (121; 216)	37.7 (29.3; 48.7)	11.6 (9.53; 14.1)	13.1 (9.60; 17.8)	56.6 (41.5; 77.2)
C								
% $\geq 1:8$ (Seroprotection)	88.2 (83.1; 92.2)	73.4 (66.9; 79.2)	98.3 (90.8; 100)	99.3 (96.2; 100)	71.4 (64.0; 78.1)	47.9 (40.2; 55.7)	51.6 (38.6; 64.5)	85.3 (78.0; 90.9)
% Seroresponse	-	-	77.6 (64.7; 87.5)	93.1 (87.7; 96.6)	-	-	8.1 (2.7; 17.8)	55.0 (46.0; 63.8)
hSBA GMT	84.8 (64.0; 112)	17.7 (14.3; 21.9)	206 (126; 339)	638 (496; 820)	26.7 (19.8; 36.0)	8.47 (6.76; 10.6)	11.1 (7.17; 17.1)	56.0 (39.7; 78.9)
W								
% $\geq 1:8$ (Seroprotection)	78.8 (72.6; 84.1)	66.8 (60.1; 73.1)	89.7 (78.8; 96.1)	98.6 (95.1; 99.8)	60.1 (52.3; 67.6)	39.6 (32.2; 47.4)	46.8 (34.0; 59.9)	80.8 (72.9; 87.2)
% Seroresponse	-	-	70.7 (57.3; 81.9)	90.3 (84.3; 94.6)	-	-	6.5 (1.8; 15.7)	49.2 (40.4; 58.1)
hSBA GMT	28.0 (22.2; 35.3)	14.2 (11.6; 17.4)	118 (64.0; 216)	419 (317; 553)	14.7 (11.0; 19.8)	6.54 (5.28; 8.11)	9.89 (6.45; 15.2)	31.0 (22.6; 42.6)
Y								
% $\geq 1:8$	92.5 (88.0; 96.0)	68.2 (61.5; 74.9)	94.8 (85.6; 99.0)	100 (97.5; 100)	65.5 (57.8; 73.2)	40.8 (33.3; 48.3)	45.2 (32.5; 57.9)	81.5 (73.8; 89.2)

(Seroprotection)	95.6)	74.4)	98.9)	100)	72.6)	48.6)	58.3)	87.8)
% Seroresponse	-	-	72.4 (59.1; 83.3)	92.4 (86.8; 96.2)	-	-	8.1 (2.7; 17.8)	49.2 (40.4; 58.1)
hSBA GMT	65.3 (51.8; 82.2)	15.3 (12.3; 19.1)	151 (83.4; 274)	566 (433; 740)	19.6 (14.4; 26.7)	7.49 (5.72; 9.82)	11.1 (6.31; 19.4)	40.5 (29.0; 56.4)

* Clinical trial identifier: NCT02842866

Clinical trial identifier: NCT04142242

^N calculated using full analysis set for persistence (FAS3) with valid serology results; Post primary dose = D30 of MET49, Pre-booster dose = D0 of MEQ00066

§N calculated using per protocol analysis Set 2 and 1 (PPAS2 and PPAS1) with valid serology results. The number of participants varies depending on the timepoints and serogroup; Post booster dose = D06 or D30 of MEQ00066

Vaccine seroresponse - titer is < 1:8 at baseline with post-vaccination titer ≥ 1:16 or titer is ≥ 1:8 at baseline with a ≥ 4-fold increase at post-vaccination.

95% CI of the single proportion calculated using the exact binomial method.

6-7 year persistence

The antibody persistence was assessed according to the vaccine (MenQuadfi or MenACWY-PS) subjects had received 6-7 years previously in study MET44 (Table 13).

For all serogroups, hSBA GMTs were higher at D30 post-primary dose than at D0 pre-booster dose for MenQuadfi-primed adults. The pre-booster GMTs were higher than the pre-primary dose for serogroup C, W, and Y in MenQuadfi-primed adults, indicative of long-term persistence of immune response for these serogroups, and were comparable for serogroup A.

Table 13: Comparison of bactericidal antibody persistence in adults (≥59 years) primed with MenQuadfi or MenACWY-PS 6-7 years before in MET44[^] – (study MEQ00066#)

Endpoint by Serogroup	6-7 years Persistence [^]			
	MenQuadfi primed (95% CI)		MenACWY-PS primed (95% CI)	
	D30 - Post primary dose\$ N=58	D0 - Pre-booster dose# N=59	D30 - Post primary dose\$ N=26	D0 - Pre-booster dose# N=26
A				
% ≥1:8 (Seroprotection)	91.4 (81.0; 97.1)	55.9 (42.4; 68.8)	76.9 (56.4; 91.0)	50.0 (29.9; 70.1)
GMT	48.0 (30.6; 75.4)	9.00 (6.44; 12.6)	27.3 (13.8; 54)	9.64 (5.18; 17.9)
C				
% ≥1:8 (Seroprotection)	74.1 (61.0; 84.7)	59.3 (45.7; 71.9)	76.9 (56.4; 91.0)	42.3 (23.4; 63.1)
GMT	52.2 (27.4; 99.7)	11.9 (7.67; 18.5)	23.9 (11.9; 48.1)	7.58 (4.11; 14.0)
W				
% ≥1:8 (Seroprotection)	75.9 (62.8; 86.1)	66.1 (52.6; 77.9)	73.1 (52.2; 88.4)	38.5 (20.2; 59.4)
GMT	31.2 (18.8; 52.0)	11.9 (7.97; 17.8)	18.8 (10.1; 34.9)	4.95 (3.39; 7.22)
Y				
% ≥1:8 (Seroprotection)	81.0 (68.6; 90.1)	59.3 (45.7; 71.9)	73.1 (52.2; 88.4)	46.2 (26.6; 66.6)
GMT	45.8 (26.9; 78.0)	11.2 (7.24; 17.5)	25.9 (12.4; 53.8)	7.19 (4.09; 12.6)

[^]Clinical trial identifier: NCT01732627

#Clinical trial identifier: NCT04142242

N: number of subjects in full analysis set for persistence (FAS3) with valid serology results.

\$ Post primary dose = D30 of MET44

Pre-booster dose = D0 of MEQ00066

95% CI of the single proportion calculated from the exact binomial method.

Booster response in adolescents and adults at least 15 years of age primed with other MenACWY vaccines

Study MET56 (NCT02752906) compared the immunogenicity of a booster dose of MenQuadfi with a booster dose of MenACWY-DT in subjects at least 15 years of age. These subjects were primed with a quadrivalent meningococcal conjugate vaccine (MenACWY-CRM (11.3%) or with MenACWY-DT (86.3%)) 4 to 10 years earlier. At baseline, hSBA seroprotection and GMT were similar for serogroups A, C, W, and Y.

Table 14: Comparison of bactericidal antibody responses to MenQuadfi and MenACWY-DT 30 days after booster vaccination in subjects at least 15 years of age primed with MenACWY-CRM or MenACWY-DT 4 to 10 years earlier (study MET56*)

Endpoint by Serogroup	MenQuadfi (95% CI)		MenACWY-DT (95% CI)	
A	N=384		N=389	
% ≥1:8 (Seroprotection)	100.0	(99.0; 100.0)	99.0	(97.4; 99.7)
% Seroresponse**	92.2	(89.0; 94.7)	87.1	(83.4; 90.3)
hSBA GMT	497	(436; 568)	296	(256; 343)
C	N=384		N=389	
% ≥1:8 (Seroprotection)	99.5	(98.1; 99.9)	99.0	(97.4; 99.7)
% Seroresponse**	97.1	(94.9; 98.6)	91.8	(88.6; 94.3)
hSBA GMT	2,618	(2,227; 3,078)	599	(504; 711)
W	N=384		N=389	
% ≥1:8 (Seroprotection)	100.0	(99.0; 100.0)	99.7	(98.6; 100.0)
% Seroresponse**	98.2	(96.3; 99.3)	90.7	(87.4; 93.4)
hSBA GMT	1,747	(1,508; 2,025)	723	(614; 853)
Y	N=384		N=389	
% ≥1:8 (Seroprotection)	99.7	(98.6; 100.0)	99.5	(98.2; 99.9)
% Seroresponse**	97.4	(95.3; 98.7)	95.6	(93.1; 97.4)
hSBA GMT	2,070	(1,807; 2,371)	811	(699; 941)

* Clinical trial identifier NCT02752906

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

** Non-inferiority criterion met.

Pharmacokinetic properties

No pharmacokinetic studies have been performed.

Preclinical safety data

Non-clinical safety data revealed no special risks for humans based on a developmental and reproductive toxicity study in female rabbits.

The administration of MenQuadfi to female rabbits at a full human dose showed no effects on mating performance, female fertility, no teratogenic potential, and no effect on pre- or post-natal development.

PHARMACEUTICAL PARTICULARS

List of excipients

- Sodium chloride
- Sodium acetate
- Water for injections

Incompatibilities

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

Expiry date

Do not use later than the date of expiry

Special precautions for storage

Store in a refrigerator (2°C – 8°C). Do not freeze.

Special precautions for disposal and other handling

The vaccine should be inspected visually for any particulate matter and/or variation of physical aspect (or discolouration) prior to administration. In the event of either being observed, discard the vaccine.

Preparation

Remove the flip off seal and using a suitable syringe and needle, withdraw 0.5 mL of solution, ensuring no air bubbles are present before injection.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Packaging Presentation

Box, 1 vial @ 0.5 ml (1 dose)
Reg No. DKI2316500543A1

HARUS DENGAN RESEP DOKTER

Pada proses pembuatannya bersinggungan dengan bahan bersumber babi

DNA babi tidak terdeteksi pada produk akhir

Manufactured by:

Sanofi Pasteur

One Discovery Drive Swiftwater PA 18370 United States

Secondary Packaged & Registered by:

PT Kalventis Sinergi Farma, Jakarta-Indonesia

Date of revision: Jan 2025 (update CCDS V6) (based on EU SmPC approved Dec 2022)

Lembaran Dalam Kemasan: Informasi Untuk Pasien

sanofi

MenQuadfi™

Meningococcal group A, C, W and Y conjugate vaccine
Larutan injeksi

Vaksin ini memerlukan pengawasan tambahan. Ini akan memberikan identifikasi yang cepat atas informasi keselamatan yang baru. Anda dapat membantu dengan melaporkan efek samping yang mungkin Anda dapatkan. Lihat bagian akhir dari Bagian 4 tentang bagaimana melaporkan efek samping.

Baca brosur ini secara hati-hati sebelum Anda atau anak Anda divaksinasi karena berisi informasi penting bagi Anda.

- Simpan brosur ini, mungkin Anda perlu membaca brosur ini kembali.
- Jika ada pertanyaan lebih lanjut, tanyakanlah kepada dokter, apoteker atau perawat Anda.
- Vaksin ini diresepkan untuk Anda atau anak Anda. Jangan diberikan pada orang lain.
- Jika ada efek samping pada Anda atau anak Anda, bicarakanlah pada dokter, apoteker atau perawat. Hal ini termasuk kemungkinan efek samping apapun yang tidak tercantum dalam selebaran ini. Lihat Bagian 4.

Ada apa dalam selebaran ini

1. Apa itu MenQuadfi dan digunakan untuk apa
2. Hal yang perlu Anda ketahui sebelum Anda atau anak Anda menggunakan MenQuadfi
3. Bagaimana cara menggunakan MenQuadfi
4. Efek samping yang mungkin terjadi
5. Bagaimana cara menyimpan MenQuadfi
6. Isi dari kemasan dan informasi lainnya

1. Apa itu MenQuadfi dan digunakan untuk apa

Untuk apa MenQuadfi digunakan

MenQuadfi adalah vaksin yang dapat diberikan kepada anak-anak mulai usia 12 bulan, remaja dan dewasa.

MenQuadfi membantu melindungi dari infeksi yang disebabkan oleh sejenis bakteri (kuman) yang disebut "*Neisseria meningitidis*", khususnya terhadap tipe A, C, Y and W-135 bagi yang bepergian ke atau tinggal di daerah dengan tingkat endemik penyakit meningokokus yang tinggi atau yang berisiko tinggi terpapar *Neisseria meningitidis* tipe A, C, Y, and W-135.

Bakteri *Neisseria meningitidis* (juga disebut *meningococci*) dapat ditularkan dari orang ke orang dan dapat menyebabkan infeksi yang serius dan terkadang mengancam jiwa, seperti:

- Meningitis - peradangan jaringan yang membungkus otak dan sumsum tulang belakang;
- Septikemia - Infeksi bakteri Meningokokus di dalam darah

Kedua infeksi tersebut dapat menyebabkan penyakit serius dengan efek jangka panjang atau kemungkinan kematian.

MenQuadfi harus digunakan sesuai dengan pedoman nasional resmi.

Bagaimana vaksin bekerja

MenQuadfi bekerja dengan cara merangsang pertahanan alami (sistem kekebalan) orang yang divaksinasi, untuk menghasilkan antibodi untuk melawan bakteri.

MenQuadfi hanya membantu melindungi dari penyakit yang disebabkan oleh *Neisseria meningitidis* tipe A, C, W dan Y.

- MenQuadfi tidak melindungi dari infeksi yang disebabkan oleh jenis *Neisseria meningitidis* lainnya.
- MenQuadfi tidak melindungi dari meningitis atau septikemia yang disebabkan oleh bakteri atau virus lain.

Seperti halnya vaksin lainnya, MenQuadfi mungkin tidak sepenuhnya melindungi semua orang yang divaksinasi.

2. Hal yang perlu Anda ketahui sebelum Anda atau anak Anda menggunakan MenQuadfi

Jangan gunakan MenQuadfi:

Jika alergi terhadap salah satu zat aktif atau bahan lain dari vaksin ini (tercantum di bagian 6) atau pernah mengalami reaksi alergi sebelumnya terhadap vaksin ini.

Jika Anda tidak yakin, bicarakan dengan dokter, apoteker atau perawat Anda sebelum Anda atau anak Anda diberikan MenQuadfi.

Peringatan dan pencegahan

Bicarakan dengan dokter, apoteker atau perawat Anda sebelum melakukan vaksinasi dengan MenQuadfi jika Anda atau anak Anda memiliki:

- infeksi dengan suhu tinggi (lebih dari 38°C). Jika demikian, vaksinasi dapat diberikan setelah infeksi terkendali. Tidak perlu menunda vaksinasi untuk infeksi ringan seperti flu. Namun, bicarakan dengan dokter, apoteker atau perawat Anda terlebih dahulu.
- masalah perdarahan atau mudah memar.
- pernah pingsan karena suntikan. Pingsan, terkadang disertai jatuh, dapat terjadi (kebanyakan pada remaja) setelah, atau bahkan sebelum, suntikan apapun.
- sistem kekebalan yang lemah (seperti karena infeksi HIV, penyakit lain, atau penggunaan obat yang mempengaruhi sistem kekebalan), karena Anda atau anak Anda mungkin tidak mendapatkan manfaat penuh dari MenQuadfi.

Jika salah satu hal di atas berlaku untuk Anda atau anak Anda (atau Anda tidak yakin apakah Anda atau anak Anda memiliki hal tersebut), bicarakan dengan dokter, apoteker atau perawat Anda sebelum Anda atau anak Anda diberikan MenQuadfi.

Seperti halnya vaksin lainnya, MenQuadfi mungkin tidak sepenuhnya melindungi semua orang yang mendapatkan vaksin.

Obat-obat lain dan MenQuadfi

Beri tahu dokter, apoteker, atau perawat Anda jika Anda atau anak Anda sedang minum, baru saja minum atau mungkin menggunakan vaksin atau obat lain, termasuk obat yang diperoleh tanpa resep.

Secara khusus, beri tahu dokter, apoteker, atau perawat Anda jika Anda atau anak Anda mengonsumsi obat yang mempengaruhi sistem kekebalan Anda, seperti:

- kortikosteroid dosis tinggi
- kemoterapi.

MenQuadfi dapat diberikan bersamaan dengan vaksin lain di tempat suntikan terpisah selama kunjungan yang sama. Ini termasuk vaksin yang melindungi dari campak, gondongan, rubella, varicella,

difteri, tetanus, pertusis, polio, *Haemophilus influenzae* tipe b, hepatitis B, *pneumococcal* dan infeksi *human papillomavirus*.

Kehamilan dan menyusui

Jika Anda sedang hamil, menyusui, merasa Anda mungkin hamil, atau berencana untuk memiliki bayi, mintalah saran kepada dokter, apoteker, atau perawat Anda sebelum menggunakan MenQuadfi.

Efek dalam kemampuan mengendarai dan mengoperasikan mesin

MenQuadfi mungkin tidak memengaruhi kemampuan Anda untuk mengemudi, bersepeda, atau menggunakan mesin. Namun, jangan mengemudi, bersepeda, atau menggunakan mesin apa pun jika Anda merasa tidak enak badan.

MenQuadfi mengandung natrium

Obat ini mengandung kurang dari 1 mmol natrium (23 mg) per dosis, dengan kata lain 'bebas natrium'.

3. Bagaimana menggunakan MenQuadfi

MenQuadfi diberikan oleh dokter atau perawat sebanyak 0,5 ml melalui suntikan di otot. Vaksin ini diberikan di lengan atas atau di paha tergantung pada usia dan seberapa besar otot yang Anda atau anak Anda miliki.

Jika Anda berisiko tinggi terpapar serogrup A dan telah mendapat dosis MenQuadfi lebih dari satu tahun yang lalu, Anda mungkin memerlukan dosis *booster*.

4. Efek samping yang mungkin terjadi

Seperti semua obat-obatan, vaksin ini dapat menyebabkan efek samping, meskipun tidak semua orang mendapatkan efek tersebut.

Jika Anda atau anak Anda mengalami gejala berikut setelah vaksinasi:

- ruam kulit yang gatal
- sesak napas
- pembengkakan pada wajah atau lidah.

Segera hubungi dokter Anda. Ini bisa jadi merupakan tanda reaksi alergi.

Kemungkinan efek samping pada anak-anak berusia 12 hingga 23 bulan:

Sangat umum (dapat mempengaruhi lebih dari 1 dari 10 anak)

- nyeri tekan, kemerahan, atau bengkak di tempat suntikan diberikan
- merasa mudah tersinggung
- menangis
- kehilangan selera makan
- merasa mengantuk

Umum (dapat mempengaruhi hingga 1 dari 10 anak)

- demam
- muntah
- diare

Jarang (dapat mempengaruhi hingga 1 dari 100 orang):

- kesulitan tidur
- gatal-gatal
- gatal, memar, kaku, atau ruam di tempat suntikan diberikan

Kemungkinan efek samping pada anak-anak (usia 2 tahun ke atas), remaja dan dewasa:

Sangat umum (dapat mempengaruhi lebih dari 1 dari 10 orang)

- Nyeri saat injeksi
- nyeri otot
- sakit kepala
- umumnya merasa tidak enak badan

Umum (dapat mempengaruhi hingga 1 dari 10 orang)

- kemerahan atau bengkak di tempat suntikan diberikan
- demam

Jarang (dapat mempengaruhi hingga 1 dari 100 orang)

- Gatal, hangat, memar atau ruam dimana suntikan diberikan
- muntah
- merasa pusing
- mual
- kelelahan (merasa lelah)

Langka (dapat mempengaruhi hingga 1 dari 1.000 orang)

- kelenjar getah bening membesar
- diare, sakit perut
- gatal-gatal, gatal, ruam
- nyeri di lengan atau kaki
- menggigil, nyeri di ketiak
- ketegasan situs injeksi

Pelaporan efek samping

Jika Anda atau anak Anda mendapatkan efek samping, bicarakanlah dengan dokter, apoteker atau perawat Anda. Termasuk kemungkinan efek samping yang tidak tercantum dalam brosur ini.

Anda juga dapat melaporkan efek samping secara langsung ke Industri Farmasi dengan kontak berikut farmakovigilans@kalventis.com.

Dengan melaporkan efek samping Anda dapat membantu memberikan informasi tentang keamanan obat ini.

5. Bagaimana cara menyimpan MenQuadfi

Jauhkan vaksin ini dari pandangan dan jangkauan anak-anak.

Jangan gunakan vaksin ini setelah tanggal kedaluwarsa yang tercantum pada karton setelah EXP.

Simpan dalam lemari pendingin (2°C – 8°C). Jangan dibekukan.

Jangan membuang obat apa pun melalui air limbah atau limbah rumah tangga. Tanyakanlah pada apoteker Anda bagaimana membuang obat-obatan yang tidak lagi Anda gunakan. Langkah-langkah ini akan membantu melindungi lingkungan.

6. Isi dari kemasan dan informasi lainnya

Apa isi dari Menquadfi

Satu dosis (0.5 ml) mengandung:

- | | |
|---|---------------|
| - Bahan aktif: | |
| - <i>Neisseria meningitidis</i> group A polysaccharide ¹ | 10 micrograms |
| - <i>Neisseria meningitidis</i> group C polysaccharide ¹ | 10 micrograms |
| - <i>Neisseria meningitidis</i> group Y polysaccharide ¹ | 10 micrograms |
| - <i>Neisseria meningitidis</i> group W polysaccharide ¹ | 10 micrograms |
| - ¹ Conjugated to tetanus toxoid carrier protein | 55 micrograms |

- Bahan tambahan:
 - sodium chloride
 - sodium acetate
 - water for injections

Seperti apa Menquadfi dan isi kemasannya

MenQuadfi berbentuk cairan injeksi, bening, tidak berwarna

MenQuadfi tersedia dalam kemasan Dus, 1 vial @ 0.5 ml dan Dus, 5 vial @0.5 ml.

Kemasan :

Dus, 1 vial @ 0.5 ml (1 dosis) dan

No. Registrasi.: DK12316500543A1

Diproduksi oleh :

Sanofi Pasteur

One Discovery Drive Swiftwater PA 18370 United States

Dikemas Sekunder dan Didaftarkan oleh:

PT Kalventis Sinergi Farma

Jakarta, Indonesia

Harus Dengan Resep Dokter

Pada proses pembuatannya bersinggungan dengan bahan bersumber babi
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DNA babi tidak terdeteksi pada produk akhir