طبقا لقرار اللجنة العلمية المتخصصة للمستحضرات الحيوية ودعوة
أعضاء اللجنة العلمية المتخصصة لطب الأطفال بجلستها في ١٧/٤ ٢٠٢٤

MenQuadfi®

Meningococcal (Groups A, C, Y, W) Conjugate Vaccine

Solution for Intramuscular Injection

INDICATIONS AND USAGE

MenQuadfi® is a vaccine indicated for active immunization for the prevention of invasive meningococcal disease caused by *Neisseria meningitidis* serogroups A, C, W, and Y. MenQuadfi is indicated for use in individuals 2 years of age and older.

MenQuadfi does not prevent *N. meningitidis* serogroup B disease.

هيئة الدواء المصرية
الإدارة المركزية للمستحضرات الحيوية واللقاحات
والدراسات الإكلينيكية
إدارة تسجيل المستحضرات الحيوية
نشرة معتمدة: من
تاريخ: ٢٠٢٤/٧/٧

DOSAGE AND ADMINISTRATION

Preparation for Administration

MenQuadfi is a clear, colorless solution.

Parenteral drug products should be inspected visually for particulate matter and/or discoloration prior to administration, whenever solution and container permit. If any of these conditions exist, the vaccine should not be administered. Discard the vial with any unused portion.

Dose and Schedule

Administer MenQuadfi as a single 0.5 mL injection intramuscularly.

Primary Vaccination

- Individuals 2 years of age and older receive a single dose.

Booster Vaccination

- A single dose of MenQuadfi may be administered to individuals 13 years of age and older who are at continued risk for meningococcal disease if at least 3 years have elapsed since a prior dose of meningococcal (groups A, C, W, Y) conjugate vaccine.

Vaccination Following Prior Dose of Meningococcal Polysaccharide Vaccine

- A single dose of MenQuadfi may be administered if at least 3 years have elapsed since a prior dose of meningococcal polysaccharide vaccine.

DOSAGE FORMS AND STRENGTHS

MenQuadfi is a sterile solution for intramuscular injection supplied in 0.5 mL single-dose vials.

CONTRAINDICATIONS

Severe allergic reaction to any component of the vaccine, or after a previous dose of MenQuadfi or any other tetanus toxoid-containing vaccine [*see Description*].

WARNINGS AND PRECAUTIONS

Management of Acute Allergic Reactions

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

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

Persons with certain complement deficiencies and persons receiving treatment that inhibits terminal complement activation (for example, eculizumab) are at increased risk for invasive disease caused by *N. meningitidis*, including invasive disease caused by serogroups A, C, W, and Y, even if they develop antibodies following vaccination with MenQuadfi [*see Clinical Pharmacology*].

Syncope

Syncope (fainting) can occur following, or even before, vaccination with MenQuadfi.

Procedures should be in place to prevent falling and injury and to manage syncope.

Guillain-Barré Syndrome

Guillain-Barré syndrome (GBS) has been reported in temporal relationship following administration of another meningococcal quadrivalent polysaccharide conjugate vaccine. The decision by the healthcare professional to administer MenQuadfi to persons with a history of GBS should take into account the expected benefits and potential risks.

Tetanus Immunization

Immunization with MenQuadfi does not substitute for routine tetanus immunization.

Limitations of Vaccine Effectiveness

Vaccination with MenQuadfi may not protect all vaccine recipients.

ADVERSE REACTIONS

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trial(s) of a vaccine cannot be directly compared to rates in the clinical trial(s) of another vaccine and may not reflect the rates observed in practice.

The safety of a single dose of MenQuadfi in individuals 2 years of age and older was evaluated in seven randomized, active-controlled, multi-center clinical studies conducted in the US and

Puerto Rico. In these studies, a total of 5,787 participants received either a primary dose (N = 4517), a booster dose (N = 1119) of MenQuadfi following priming with a meningococcal conjugate vaccine, or a dose of MenQuadfi following a prior dose of meningococcal polysaccharide vaccine (N = 151) and were included in the safety analyses.

Safety Monitoring

Participants were monitored for immediate reactions for 30 minutes following vaccination while at the study site. Solicited injection site and systemic reactions were recorded by participants or by parents/guardians in a diary card at home daily for 7 days following vaccination. All unsolicited adverse events that occurred within 30 days following vaccination were recorded by participants or by parents/guardians and collected by the study site at the next visit. Unsolicited adverse events that were medically attended (i.e., visits to an emergency room, or an unexpected visit to a health care provider), and all serious adverse events (SAEs) were collected for at least 6 months after vaccination for all studies except Study 7 [NCT04142242], in which these safety data were collected for at least 1 month.

Primary Vaccination

Children 2 through 9 years of age

The safety of MenQuadfi in children 2 years through 9 years of age was evaluated in Study 1 (NCT03077438). The safety analysis set included 498 participants who received MenQuadfi and 494 participants who received Meningococcal (Groups A, C, Y, and W-135) Oligosaccharide Diphtheria CRM_{197} Conjugate Vaccine (MenACWY-CRM). Of the participants 2 through 9 years of age who received MenQuadfi (N = 498), 50.2% were 2 through 5 years of age, 49.8% were 6 through 9 years of age, 49.0% were female, 80.5% were White, 13.3% were Black or African American, 0.4% were Asian, 5.2% were of other racial groups, and 22.9% were of Hispanic or Latino ethnicity. There were no substantive differences in demographic characteristics between the vaccine groups.

The most common solicited injection site reaction was pain (38.6% in the MenQuadfi group and 42.4% in the MenACWY-CRM group), followed by erythema (22.6% in the MenQuadfi group and 31.5% in the MenACWY-CRM group) and swelling (13.8% in the MenQuadfi group and 21.5% in the MenACWY-CRM group). The most common solicited systemic reactions were myalgia (20.1% in the MenQuadfi group and 23.0% in the MenACWY-CRM group) and malaise (21.1% in the MenQuadfi group and 20.4% in the MenACWY-CRM group) followed by headache (12.5% in the MenQuadfi group and 11.5% in the MenACWY-CRM group). A low percentage of participants reported fever (1.9% in the MenQuadfi group and 2.7% in the MenACWY-CRM group). Most adverse reactions were mild to moderate in severity.

SAEs occurred at a rate of 1.4% following MenQuadfi and at a rate of 0.6% following MenACWY-CRM during the entire study period. Most SAEs occurred more than 30 days following vaccination and were commonly occurring events in the general population in this age group. No SAEs were determined to be vaccine related.

Adolescents 10 through 17 years of age

The safety of MenQuadfi in adolescents 10 through 17 years of age was evaluated in two clinical trial studies Study 2 (NCT02199691) and Study 3 (NCT02842853). The safety analysis set in these two studies included 3,196 participants who received MenQuadfi alone (1,684 participants), MenQuadfi concomitantly with Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine, Adsorbed (Tdap) and Human Papillomavirus Quadrivalent (Types 6, 11, 16, and 18) Vaccine, Recombinant (HPV) (392 participants), the concomitant vaccines without MenQuadfi (296 participants), or a U.S.-licensed comparator meningococcal vaccine (824 participants). The comparator meningococcal vaccine was either MenACWY-CRM (501 participants) or (Meningococcal (Groups A, C, Y, and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine) (MenACWY-DT) (323 participants).

Of the participants 10 through 17 years of age who received MenQuadfi (N = 1,684), 49.6% were female. Among those with reported race and ethnicity, 79.3% were White, 14.2% were Black or African American, 1.1% were Asian, 5.4% were of other racial groups, and 21.5% were of Hispanic or Latino ethnicity. Mean age was 11.9 years at time of administration. There were no substantive differences in demographic characteristics between the vaccine groups.

The most common solicited injection site reaction was pain (45.2% and 34.8% in the MenQuadfi group in Studies 2 and 3, 42.5% in the MenACWY-CRM group in Study 2, and 41.4% in the MenACWY-DT group in Study 3), followed by erythema (5.0% and 4.5% in the MenQuadfi group in Studies 2 and 3, 7.5% in the MenACWY-CRM group in Study 2, and 4.5% in the MenACWY-DT group in Study 3) and swelling (5.4% and 4.1% in the MenQuadfi group in Studies 2 and 3, 6.5% in the MenACWY-CRM group in Study 2, and 4.8% in the MenACWY-DT group in Study 3). The most common solicited systemic reactions were myalgia (35.3% and 27.4% in the MenQuadfi group in Studies 2 and 3, 35.2% in the MenACWY-CRM group in Study 2, and 31.2% in the MenACWY-DT group in Study 3) and headache (30.2% and 26.5% in the MenQuadfi group in Studies 2 and 3, 30.9% in the MenACWY-CRM group in Study 2, and 28.0% in the MenACWY-DT group in Study 3) followed by malaise (26.0% and 19.4% in the MenQuadfi group in Studies 2 and 3, 26.4% in the MenACWY-CRM group in Study 2, and 23.9% in the MenACWY-DT group in Study 3). A low percentage of participants reported fever (1.4% and 0.7% in the MenQuadfi group in Studies 2 and 3, 1.2% in the MenACWY-CRM group in Study 2, and 0.6% in the MenACWY-DT group in Study 3). Most adverse reactions were mild to moderate in severity.

Among 296 participants who received Tdap and HPV concomitantly (without MenQuadfi) and 392 participants who received MenQuadfi concomitantly with Tdap and HPV, there were no notable differences in the rates of systemic solicited adverse reactions within 7 days following vaccination.

Dizziness within 30 minutes following vaccination was experienced by 1 (0.2%) participant who received MenQuadfi in Study 2(NCT02199691) and 2 (0.2%) participants who received MenQuadfi in Study 3 (NCT02842853). Three participants in Study 2 experienced syncope within 30 minutes following vaccination: 1 (0.2%) participant who received MenACWY-CRM, 1 (0.3%) participant who received MenQuadfi concomitantly with Tdap and HPV, and 1 (0.3%) participant who received Tdap and HPV concomitantly (without MenQuadfi). These events were non-serious and spontaneously resolved on the same day.

In Study 2, SAEs occurred at a rate of 0.8% following MenQuadfi and 0.8% following MenACWY-CRM. In Study 3, SAEs occurred at a rate of 0.3% following MenQuadfi and 0.9% following MenACWY-DT. No SAEs were determined to be vaccine related.

Adults 18 through 55 years of age

The safety of MenQuadfi in adults 18 through 55 years of age was evaluated in Study 3 (NCT02842853). The safety analysis set included 1,495 participants who received MenQuadfi and 312 participants who received MenACWY-DT. Of the participants 18 years through 55 years of age who received MenQuadfi (N = 1,495), 65.2% were female. Among those with reported race and ethnicity, 73.3% were White, 21.0% were Black or African American, 2.2% were Asian, 3.5% were of other racial groups, and 20.0% were of Hispanic or Latino ethnicity. Mean age was 39.4 years at time of administration.

The most common solicited injection site reaction was pain (41.9% in the MenQuadfi group and 35.0% in the MenACWY-DT group), followed by erythema (5.1% in the MenQuadfi group and 3.7% in the MenACWY-DT group) and swelling (4.3% in the MenQuadfi group and 3.4% in the MenACWY-DT group). The most common solicited systemic reactions were myalgia (35.6% in the MenQuadfi group and 31.2% in the MenACWY-DT group) followed by headache (29.0% in the MenQuadfi group and 27.6% in the MenACWY-DT group) and malaise (22.9% in the MenQuadfi group and 18.9% in the MenACWY-DT group). A low percentage of participants reported fever (1.4% in the MenQuadfi group and 1.7% in the MenACWY-DT group). Most adverse reactions were mild to moderate in severity.

Dizziness within 30 minutes following vaccination was experienced by 5 (0.3%) participants who received MenQuadfi and 1 (0.3%) participant who received MenACWY-DT. These events were non-serious and spontaneously resolved on the same day.

SAEs occurred at a rate of 1.6% following MenQuadfi and at a rate of 0.6% following MenACWY-DT during the entire study period. No SAEs were determined to be vaccine related.

Adults 56 years of age and older

The safety of MenQuadfi in adults 56 years of age and older was evaluated in Study 4 (NCT02842866). The safety analysis set included 448 participants who received MenQuadfi intramuscularly and 453 participants who received a non-conjugate comparator meningococcal vaccine (Meningococcal Polysaccharide Vaccine, Groups A, C, Y, and W-135 Combined – MenACWY-PS, Sanofi Pasteur) subcutaneously. Of the participants 56 years of age and older who received MenQuadfi (N = 448), 44.4% were 56 through 64 years of age, 55.6% were 65 years of age and older, 57.6% were female, 86.6% were White, 11.6% were Black or African American, 1.1% were Asian, 0.4% were of other racial groups and 7.8% were of Hispanic or Latino ethnicity. Mean age was 67.0 years at time of administration.

The most common solicited injection site reaction was pain (25.5% in the MenQuadfi group and 9.6% in the MenACWY-PS group), followed by erythema (5.2% in the MenQuadfi group and 0.0% in the MenACWY-PS group) and swelling (4.5% in the MenQuadfi group and 0.0% in the MenACWY-PS group). The most common solicited systemic reactions were myalgia (21.9% in the MenQuadfi group and 15.3% in the MenACWY-PS group) followed by headache (19.0% in the MenQuadfi group and 14.6% in the MenACWY-PS group) and malaise (14.5% in the

MenQuadfi group and 11.3% in the MenACWY-PS group). A low percentage of participants reported fever (2.1% in the MenQuadfi group and 0.4% in the MenACWY-PS group). Most adverse reactions were mild to moderate in severity.

SAEs occurred at a rate of 3.3% following MenQuadfi and at a rate of 3.3% following MenACWY-PS during the entire study period. No SAEs were determined to be vaccine related.

Booster Vaccination Following Priming with a Meningococcal Conjugate Vaccine; Vaccination Following a Prior Dose of a Meningococcal Polysaccharide Vaccine

Adolescents and adults 15 years of age and older

The safety of MenQuadfi in previously vaccinated adolescents and adults 15 years of age and older was evaluated in Study 5 (NCT02752906). All randomized participants had received a primary dose of either (MenACWY-CRM or MenACWY-DT) 4 to 10 years previously. The safety analysis set included 402 participants who received a single booster dose of MenQuadfi (median age: 17.8 years) and 407 participants who received a single booster dose of MenACWY-DT (median age: 17.9 years). Of the participants who received MenQuadfi, 51.5% were female, 85.1% were White, 9.7% were Black, 2.7 % were Asian and 2.2 % were of other racial groups, and 15.7% were of Hispanic or Latino ethnicity.

The most commonly reported solicited adverse reactions (≥10%) within 7 days of MenQuadfi booster vaccination were injection site pain (44.7%) and headache (37.9%), myalgia (36.7%), and malaise (27.6%). The majority of solicited adverse reactions were Grade 1 or 2 and resolved within 3 days. Compared with recipients of a MenACWY-DT booster dose, recipients of a MenQuadfi booster dose had higher rates of injection site erythema (MenQuadfi 5.0%, MenACWY-DT 1.5%) and swelling (MenQuadfi 4.0%, MenACWY-DT 0.7%). Overall rates of solicited adverse reactions were comparable to those observed in unvaccinated adolescents and adults after a single MenQuadfi dose.

SAEs occurred at a rate of 1.2% following MenQuadfi and at a rate of 1.0% following MenACWY-DT during the entire study period. No SAEs were determined to be vaccine related.

Adolescents and adults 13 through 26 years of age

The safety of MenQuadfi in previously vaccinated adolescents and adults 13 through 26 years of age was evaluated in Study 6 (NCT04084769). All randomized participants had received a primary dose of either MenQuadfi or MenACWY-CRM 3-6 years previously. The safety analysis set included 370 participants who received a booster dose of MenQuadfi alone (median age: 15.0 years for subjects primed with MenQuadfi and 16.0 years for subjects primed with MenACWY-CRM) and 185 participants who received MenQuadfi concomitantly with MenB-FHbp [Meningococcal Group B Vaccine] (N=93, median age: 15.0 years) or 4CMenB [Meningococcal Group B Vaccine] (N=92, median age: 15.0 years). Of the participants who received a booster dose of MenQuadfi, 47.2% were female, 88.1% were White, 8.2% were Black, 3.8% were of other racial groups, and 14.4% were of Hispanic or Latino ethnicity.

The most common solicited injection site reaction was pain (38.2% in the MenQuadfi in MenQuadfi-primed group, 33.7% in the MenQuadfi in MenACWY-CRM group, 48.9% in the MenQuadfi and MenB-FHbp in MenQuadfi-primed group and 56.5% in the MenQuadfi and 4CMenB in MenQuadfi-primed group), followed by erythema (6.5%, 5.4%, 1.1% and 6.5%

respectively) and swelling (5.4%, 1.6%, 2.2% and 5.4%, respectively). The most common solicited systemic reactions were myalgia (32.8% in the MenQuadfi in MenQuadfi-primed group, 34.8% in the MenQuadfi in MenACWY-CRM group, 65.2% in the MenQuadfi and MenB-FHbp in MenQuadfi-primed group and 63.0% in the MenQuadfi and 4CMenB in MenQuadfi-primed group) followed by headache (36.0%, 34.8%, 42.4% and 39.1%, respectively) and malaise (26.9%, 25.5%, 39.1% and 40.2%, respectively). A low percentage of participants reported fever (none in the MenQuadfi in MenQuadfi-primed group, 2.2% in the MenQuadfi in MenACWY-CRM-primed group, 1.1% in the MenQuadfi and MenB-FHbp in MenQuadfi-primed group and 4.4% in the MenQuadfi and 4CMenB in MenQuadfi-primed group. Most adverse reactions were mild to moderate in severity.

There were no reported SAEs that were assessed as vaccine related.

Older adults ≥ 59 years of age

The safety of MenQuadfi in previously vaccinated older adults ≥ 59 years of age was evaluated in Study 7 (NCT04142242). All randomized participants had received a prior dose of either MenQuadfi (N=162) or MenACWY-PS (N=151) at a median interval of 3.34 and 3.35 years, respectively. The safety analysis set included 313 participants who received a dose of MenQuadfi (median age: 69.0 years for subjects primed with MenQuadfi and 70.0 years for subjects who received a prior dose of MenACWY-PS); 62.6% were female, 90.4% were White, 8.6% were Black, 0.3% were of other racial groups, and 10.5% were of Hispanic or Latino ethnicity.

The most common solicited injection site reaction was pain (16.7% in the MenQuadfi-primed group and 21.2% in the group who previously received MenACWY-PS), followed by erythema (3.7% in the MenQuadfi-primed group and 7.3% in the group who previously received MenACWY-PS) and swelling (3.7% in the MenQuadfi-primed group and 4.6% in the group who previously received MenACWY-PS). The most common solicited systemic reactions were myalgia (21.6% in the MenQuadfi-primed group and 19.9% in the group who previously received MenACWY-PS) followed by headache (18.5% in the MenQuadfi-primed group and 13.9% in the group who previously received MenACWY-PS) and malaise (13.6% in the MenQuadfi-primed group and 14.6% in the group who previously received MenACWY-PS). A low percentage of participants reported fever (0.6% in the MenQuadfi-primed group and none in the group who previously received MenACWY-PS). Most adverse reactions were mild to moderate in severity.

There were no reported SAEs that were assessed as vaccine related.

DRUG INTERACTIONS

Concomitant Administration with Other Vaccines

In a clinical trial in adolescents 10 through 17 years of age, MenQuadfi was administered concomitantly with Tdap and HPV [*see Adverse Reactions* and *Clinical Studies*].

Lower geometric mean antibody concentrations (GMCs) for antibodies to the pertussis antigens filamentous hemagglutinin (FHA), pertactin (PRN) and fimbriae (FIM) were observed when

MenQuadfi was co-administered with Tdap and HPV, compared to concomitant administration of Tdap and HPV (without MenQuadfi) [*see Clinical Studies*].

Immunosuppressive Treatments

Immunosuppressive therapies may reduce the immune response to MenQuadfi [*see Warnings and Precautions*].

USE IN SPECIFIC POPULATIONS

Pregnancy

There are no clinical studies of MenQuadfi in pregnant women. Available human data on MenQuadfi administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

A developmental toxicity study in female rabbits administered a full human dose (0.5 mL) prior to mating and during gestation period revealed no evidence of harm to the fetus due to MenQuadfi

In a developmental toxicity study, female rabbits received a human dose of MenQuadfi by intramuscular injection on five occasions: 30 days and 10 days prior to mating, gestation days 6, 12 and 27. No adverse effects on pre-weaning development up to post-natal day 35 were observed. There were no vaccine-related fetal malformations or variations observed.

Lactation

It is not known whether MenQuadfi is excreted in human milk. Data are not available to assess the effects of MenQuadfi on the breastfed infant or on milk production/excretion.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for MenQuadfi and any potential adverse effects on the breastfed child from MenQuadfi or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

Pediatric Use

Safety and effectiveness of MenQuadfi have not been established in individuals younger than 2 years of age.

Geriatric Use

A total of 249 participants 65 years of age and older, including 71 participants 75 years of age or older, in Study 4 received one dose of MenQuadfi [*see Adverse Reactions* and *Clinical Studies*].

MenQuadfi recipients ≥ 65 years of age had lower GMTs and seroresponse rates for all serogroups compared to MenQuadfi recipients 56 through 64 years of age [*see Clinical Studies*].

DESCRIPTION

MenQuadfi is a sterile liquid vaccine administered by intramuscular injection that contains *Neisseria meningitidis* serogroup A, C, W, and Y capsular polysaccharide antigens that are individually conjugated to tetanus toxoid protein. *N. meningitidis* A, C, W, and Y strains are cultured on Mueller Hinton agar medium and grown in Watson Scherp medium. The polysaccharides are extracted from the *N. meningitidis* cells and purified by centrifugation, detergent precipitation, alcohol precipitation, solvent extraction, and diafiltration. To prepare the polysaccharides for conjugation, Serogroup A is activated with carbonyldiimidazole (CDI), derivatized with adipic acid dihydrazide (ADH), and purified by diafiltration. Serogroups C, W, and Y are depolymerized, activated with periodate, and purified by diafiltration.

Clostridium tetani is fermented in media to generate tetanus toxin, which is purified by ammonium sulfate precipitation to yield purified tetanus toxin (PTT) and detoxified with formaldehyde to yield purified tetanus protein (PTP). The PTP is then concentrated and filtered to yield concentrated tetanus protein (CTP). The activated/derivatized polysaccharides are covalently linked to tetanus toxoid and purified by chromatography and serial diafiltration. The four meningococcal components, present as individual serogroup-specific glycoconjugates, compose the final formulated vaccine.

MenQuadfi is manufactured as a sterile, clear, colorless solution. Each 0.5 mL dose of vaccine contains 10 microgram each of meningococcal A, C, W, and Y polysaccharide antigens conjugated to approximately 55 micrograms tetanus toxoid protein carrier; 3.35 mg sodium chloride (0.67%), and 1.23 mg sodium acetate (30 mM). Potency of MenQuadfi is determined by quantifying the amount of each polysaccharide antigen that is conjugated to tetanus toxoid protein and the amount of unconjugated polysaccharide present.

No preservative or adjuvant is added during manufacture. Each 0.5 mL dose may contain residual amounts of formaldehyde of less than 3 mcg/mL, by calculation.

The vial in which the vaccine components are contained is composed of USP Type I borosilicate glass. The vial stopper is a chlorobutyl synthetic polyisoprene blend stopper (not made with natural rubber latex).

CLINICAL PHARMACOLOGY

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 in serum 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.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility

MenQuadfi has not been evaluated for carcinogenic or mutagenic potential or for impairment of male fertility. MenQuadfi administered to female rabbits had no effects on fertility [*see Use in Specific Populations*].

CLINICAL STUDIES

To infer effectiveness of MenQuadfi, the immunogenicity in persons 2 years of age and older was evaluated using a serogroup-specific serum bactericidal assay with exogenous human complement (hSBA). The hSBA responses following a single dose of MenQuadfi for primary vaccination were assessed in four studies, and the hSBA responses following a single dose of MenQuadfi for booster vaccination were assessed in two studies. The hSBA responses following a single dose of MenQuadfi were also assessed in one study that enrolled a group of participants who had received a prior dose of meningococcal polysaccharide vaccine. Serum was collected at baseline and 30 days post-vaccination to measure antibodies with hSBA. The hSBA geometric mean titers (GMTs) and proportion of participants who achieved hSBA seroresponse (defined below) were evaluated.

- Seroresponse rate for each serogroup: the proportion of participants with an hSBA
  - pre-vaccination titer < 1:8 who achieved a post-vaccination titer ≥ 1:16, or
  - pre-vaccination titer ≥ 1:8 who achieved a post-vaccination titer at least 4-fold greater than the pre-vaccination titer.

Primary Vaccination

Immunogenicity in Children 2 through 9 Years of Age

Immunogenicity of MenQuadfi compared to MenACWY-CRM in participants 2 through 9 years of age was evaluated in Study 1 (NCT03077438). The hSBA seroresponse rate and GMTs are presented in Table 1.

Immune non-inferiority, based on seroresponse rates, was demonstrated for MenQuadfi as compared to MenACWY-CRM for all four serogroups.

Table 1: Comparison of Bactericidal Antibody Responses to MenQuadfi and MenACWY-CRM 30 Days after Vaccination of Participants 2 through 9 Years of Age (Study 1)*

Endpoint†	MenQuadfi (95% CI)	MenACWY-CRM (95% CI)	Percent difference MenQuadfi minus MenACWY-CRM‡ (95% CI)
A	N=455-456	N=458	
% Participants achieving Seroresponse	55.4 (50.7; 60.0)	47.8 (43.2; 52.5)	7.6 (1.1, 14.0)

GMT	25 (22; 28)	23 (20; 26)	
C	N=458	N=458-459	
% Participants achieving Seroresponse	95.2 (92.8; 97.0)	47.8 (43.2; 52.5)	47.4 (42.2, 52.2)
GMT	238 (209; 270)	17.0 (14; 20)	
W	N=458	N=459	
% Participants achieving Seroresponse	78.8 (74.8; 82.5)	64.1 (59.5; 68.4)	14.8 (8.9, 20.5)
GMT	38 (34; 42)	26 (23; 30)	
Y	N=458	N=459	
% Participants achieving Seroresponse	91.5 (88.5; 93.9)	79.3 (75.3; 82.9)	12.2 (7.7, 16.7)
GMT	69 (61; 77)	44 (38; 50)	

* Clinical trial identifier NCT03077438

† Seroresponse rate (primary endpoint) for each serogroup: the proportion of participants with an hSBA pre-vaccination titer < 1:8 who achieved a post-vaccination titer ≥ 1:16, or pre-vaccination titer ≥ 1:8 who achieved a post-vaccination titer at least 4-fold greater than the pre-vaccination titer.

‡ Overall non-inferiority would be demonstrated if the lower limit of the 2-sided 95% CI is > -10% for all four serogroups.

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.

Immunogenicity in Adolescents 10 through 17 Years of Age

Immunogenicity of MenQuadfi compared to MenACWY-CRM in participants 10 through 17 years of age was evaluated in Study 2 (NCT02199691). Study 2 was conducted in healthy meningococcal vaccine naïve participants and evaluated seroresponse rates following administration with either MenQuadfi alone, MenACWY-CRM alone, MenQuadfi co-

administered with Tdap, and HPV, or Tdap and HPV alone. The hSBA seroresponse rate and GMTs for Study 2 are presented in Table 2.

Immune non-inferiority, based on seroresponse, was demonstrated for MenQuadfi as compared to MenACWY-CRM for all four serogroups.

Study 2 (NCT02199691) was conducted in healthy meningococcal vaccine naïve male and female participants and evaluated seroresponses following administration with either MenQuadfi alone; MenACWY-CRM alone; MenQuadfi co-administered with Tdap, and HPV; or Tdap and HPV alone. The hSBA seroresponse rate and GMTs for the MenQuadfi alone and MenACWY-CRM alone groups are presented in Table 2.

Table 2: Comparison of Bactericidal Antibody Responses to MenQuadfi and MenACWY-CRM 30 Days after Vaccination of Participants 10 through 17 Years of Age (Study 2)*

Endpoint†	MenQuadfi (95% CI)	MenACWY-CRM (95% CI)	Percent difference MenQuadfi minus MenACWY-CRM‡ (95% CI)
A	N=463	N=464	
% Participants achieving Seroresponse	70.2 (65.8; 74.3)	60.3 (55.7; 64.8)	9.8 (3.7; 15.9)
GMT	44 (39; 50)	35 (30; 41)	
C	N=462	N=463	
% Participants achieving Seroresponse	96.1 (93.9, 97.7)	61.6 (57.0, 66.0)	34.5 (29.7; 39.3)
GMT	387 (329; 456)	51 (41; 64)	
W	N=463	N=464	
% Participants achieving Seroresponse	84.2 (80.6; 87.4)	56.0 (51.4; 60.6)	28.2 (22.5; 33.7)

Endpoint†	MenQuadfi (95% CI)	MenACWY-CRM (95% CI)	Percent difference MenQuadfi minus MenACWY-CRM‡ (95% CI)
GMT	87 (78; 97)	36 (32; 41)	
Y	N=462-463	N=464	
% Participants achieving Seroresponse	91.1 (88.2; 93.6)	66.8 (62.3; 71.1)	24.3 (19.2; 29.3)
GMT	76 (66; 87)	28 (24; 32)	

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إدارة تسجيل المستحضرات الحيوية
نشرة معتمدة: د/ [illegible]
تاريخ: ٧/ ٧/ ٢٠٢٤

* Clinical trial identifier NCT02199691

† Seroresponse rate (primary end point) for each serogroup: the proportion of participants with an hSBA pre-vaccination titer < 1:8 who achieved a post-vaccination titer ≥ 1:16, or pre-vaccination titer ≥ 1:8 who achieved a post-vaccination titer at least 4-fold greater than the pre-vaccination titer.

‡ Overall non-inferiority would be demonstrated if the lower limit of the 2-sided 95% CI is > -10% for all four serogroups.

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.

Study 3 evaluated the immunogenicity of MenQuadfi (N=1097-1098) compared to MenACWY-DT (N=300) in healthy meningococcal-naïve participants 10 through 17 years of age. Seroresponse rates for MenQuadfi were noninferior to those of MenACWY-DT for all serogroups based on the same non-inferiority criteria defined for Study 2.

Immunogenicity in Adults 18 through 55 Years of Age

Immunogenicity of MenQuadfi compared to MenACWY-DT in participants 18 through 55 years of age was evaluated in Study 3 (NCT02842853). The hSBA seroresponse rate and GMTs are presented in Table 3.

Immune non-inferiority, based on seroresponse rates, was demonstrated for MenQuadfi as compared to MenACWY-DT for all four serogroups.

Table 3: Comparison of Bactericidal Antibody Responses to MenQuadfi and MenACWY-DT 30 Days after Vaccination of Participants 18 through 55 Years of Age (Study 3)*

Endpoint†	MenQuadfi (95% CI)	MenACWY-DT (95% CI)	Percent difference MenQuadfi minus MenACWY-DT‡ (95% CI)
A	N=1,406-1,408	N=293	

Endpoint†	MenQuadfi (95% CI)	MenACWY-DT (95% CI)	Percent difference MenQuadfi minus MenACWY-DT‡ (95% CI)
% Participants achieving Seroresponse	73.5 (71.2; 75.8)	53.9 (48.0; 59.7)	19.6 (13.5; 25.8)
GMT	106 (97; 117)	52 (43; 64)	
C	N=1,406-1,408	N=293	
% Participants achieving Seroresponse	83.4 (81.4; 85.3)	42.3 (36.6; 48.2)	41.1 (35.0; 46.9)
GMT	234 (210; 261)	37 (29; 49)	
W	N=1,408-1,410	N=293	
% Participants achieving Seroresponse	77.0 (74.7; 79.2)	50.2 (44.3; 56.0)	26.8 (20.7; 32.9)
GMT	76 (69; 83)	33 (26; 42)	
Y	N=1,408-1,410	N=293	
% Participants achieving Seroresponse	88.1 (86.3; 89.8)	60.8 (54.9; 66.4)	27.4 (21.7; 33.3)
GMT	219 (200; 239)	55 (42; 70)	

* Clinical trial identifier NCT02842853

† Seroresponse rate (primary endpoint) for each serogroup: the proportion of participants with an hSBA pre-vaccination titer < 1:8 who achieved a post-vaccination titer ≥ 1:16, or pre-vaccination titer ≥ 1:8 who achieved a post-vaccination titer at least 4-fold greater than the pre-vaccination titer.

‡ The overall non-inferiority would be demonstrated if the lower limit of the 2-sided 95% CI is > -10% for all four serogroups.

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.

Immunogenicity in Adults 56 Years of Age and Older

Immunogenicity of MenQuadfi compared to MenACWY-PS in participants 56 years and older was evaluated in Study 4 (NCT02842866).

Enrollment was stratified by age category: 56 through 64 years of age (44.3%), 65 through 74 years of age (39.7%), and 75 years of age and older (15.9%). The overall mean age of participants who received MenQuadfi was 66.9 years; range: 56 through 89.8 years of age. The mean age for participants in the 56 through 64 years age stratum who received MenQuadfi was 60.4 years, the mean age for participants ≥ 65 years age stratum who received MenQuadfi was 72.2 years.

The hSBA seroresponse rate and GMTs are presented in Table 4.

Immune non-inferiority, based on seroresponse rates, was demonstrated for MenQuadfi as compared to MenACWY-PS for all four serogroups.

Table 4: Comparison of Bactericidal Antibody Responses to MenQuadfi and MenACWY-PS in Naïve Older Adults and Elderly 30 Days after Vaccination (Study 4)*

Endpoint†	MenQuadfi (95% CI)	MenACWY-PS (95% CI)	Percent difference MenQuadfi minus MenACWY-PS‡ (95% CI)
A	N=433	N=431	
% Participants achieving Seroresponse	58.2 (53.4; 62.9)	42.5 (37.7; 47.3)	15.7 (9.08; 22.2)
GMT	55 (47; 65)	31 (27; 37)	
C	N=433	N=431	
% Participants achieving Seroresponse	77.1 (72.9; 81.0)	49.7 (44.8; 54.5)	27.5 (21.2; 33.5)
GMT	101 (84; 123)	25 (21; 30)	
W	N=433	N=431	

Endpoint†	MenQuadfi (95% CI)	MenACWY-PS (95% CI)	Percent difference MenQuadfi minus MenACWY-PS‡ (95% CI)
% Participants achieving Seroresponse	62.6 (57.8; 67.2)	44.8 (40.0; 49.6)	17.8 (11.2; 24.2)
GMT	28 (24; 33)	15 (13; 18)	
Y	N=433	N=431	
% Participants achieving Seroresponse	74.4 (70.0; 78.4)	43.4 (38.7; 48.2)	31.0 (24.6; 37.0)
GMT	69 (59; 81)	21 (17; 25)	

*Clinical trial identifier NCT02842866

† Seroresponse rate (primary endpoint) for each serogroup: the proportion of participants with an hSBA pre-vaccination titer < 1:8 who achieved a post-vaccination titer ≥ 1:16, or pre-vaccination titer ≥ 1:8 who achieved a post-vaccination titer at least 4-fold greater than the pre-vaccination titer.

‡ The overall non-inferiority would be demonstrated if the lower limit of the 2-sided 95% CI is > -10% for all four serogroups.

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.

Booster Vaccination Following Priming with a Meningococcal Conjugate Vaccine; Vaccination Following a Prior Dose of a Meningococcal Polysaccharide Vaccine

Immunogenicity in Adolescents and Adults at least 15 Years of Age and Older

Immunogenicity of a booster dose of MenQuadfi compared to a booster dose of MenACWY-DT was evaluated in Study 5 (NCT02752906). The study-enrolled participants 15 years of age and older who had received a primary dose of MenACWY-CRM or MenACWY-DT 4 to 10 years previously.

Immune non-inferiority, based on seroresponse rates, was demonstrated for MenQuadfi as compared to MenACWY-DT for all four serogroups.

For a description of study design and number of participants, see Adverse Reactions section, Booster Vaccination Following Priming with a Meningococcal Conjugate Vaccine; Vaccination Following a Prior Dose of a Meningococcal Polysaccharide Vaccine. The primary immunogenicity endpoint was hSBA seroresponse to each serogroup 30 days following booster vaccination with MenQuadfi or MenACWY-DT given to participants who received a prior dose of

MenACWY-CRM or MenACWY-DT 4 to 10 years ago. The other endpoints included the proportions of participants with post-vaccination hSBA ≥1:8 and the hSBA GMTs for each serogroup. These endpoints were also evaluated at 6 days post vaccination in a subset.

Seroresponse rates at Day 30 following booster vaccination with MenQuadfi were 92.2% for serogroup A, 97.1% for serogroup C, 98.2% for serogroup W, and 97.4% for serogroup Y, as compared to 87.1% for serogroup A, 91.8% for serogroup C, 90.7% for serogroup W, and 95.6% for serogroup Y, following booster vaccination with MenACWY-DT. At Day 6, following booster vaccination with MenQuadfi, seroresponse rates were 72.7%, 83.6%, 94.5%, and 90.9% for serogroups A, C, W, and Y, respectively.

The hSBA GMTs were 173, 334, 499, and 302 for serogroups A, C, W, and Y at Day 6, and 497, 2618, 1747, and 2070, respectively, for the 4 serogroups at Day 30 following booster dose of MenQuadfi.

Overall, similar seroresponse rates were observed for those participants who received booster vaccination with MenACWY-DT.

Immunogenicity in Adolescents and Adults 13 through 26 Years of Age

Immunogenicity of a booster dose of MenQuadfi was evaluated in Study 6 (NCT04084769). The study enrolled participants 13 through 26 years of age who had received a primary dose of MenQuadfi or MenACWY-CRM 3-6 years previously in Study 2 or Study 3.

For a description of study design and number of participants, see Adverse Reactions section, Booster Vaccination Following Priming with a Meningococcal Conjugate Vaccine; Vaccination Following a Prior Dose of a Meningococcal Polysaccharide Vaccine. The primary immunogenicity endpoints were hSBA seroresponse to each serogroup 30 days following a booster vaccination with MenQuadfi given to participants who received a prior dose of MenQuadfi or MenACWY-CRM 3-6 years previously (Table 5). The other endpoints included hSBA GMTs for each serogroup. These endpoints were also evaluated at 6 days post vaccination in a subset (Per-Protocol Analysis Set 1).

Table 5: Comparison of hSBA Seroresponse Rates 30 Days Following Booster Vaccination with MenQuadfi in Participants 13 through 26 Years of Age Primed with MenQuadfi or MenACWY-CRM 3-6 Years Previously (Study 6)*

‡Endpoint by Serogroup	MenQuadfi-primed (95% CI) N=174	MenACWY-CRM-primed (95% CI) N=176
A		
% Participants achieving Seroresponse	94.8 (90.4; 97.6)	93.2 (88.4; 96.4)

C		
% Participants achieving Seroresponse	97.1 (93.4; 99.1)	98.9 (96.0; 99.9)
W		
% Participants achieving Seroresponse	97.7 (94.2; 99.4)	98.9 (96.0; 99.9)
Y		
% Participants achieving Seroresponse	98.9 (95.9; 99.9)	100 (97.9; 100)

* Clinical trial identifier NCT04084769
N: number of subjects in Per-Protocol Analysis Set 2 (D30) with valid serology results.
‡Seroresponse rate (primary endpoint) for each serogroup: the proportion of participants with an hSBA pre vaccination titer < 1:8 who achieved a post-vaccination titer ≥ 1:16, or pre-vaccination titer ≥ 1:8 who achieved a post-vaccination titer at least 4-fold greater than the pre-vaccination titer.
Sufficiency of hSBA seroresponse after MenQuadfi vaccination was demonstrated if the lower limit of the 2-sided 95% CI was >75%.

Seroresponse rates at Day 6 following booster dose with MenQuadfi were 82.6%, 89.1%, 97.8%, and 95.7% for serogroups A, C, W, and Y, respectively, in MenQuadfi-primed participants (N=46) and 77.8%, 93.3%, 88.9%, and 91.1% for serogroups A, C, W, and Y, respectively, in MenACWY-CRM-primed participants (N=45).

Following a booster dose of MenQuadfi, the hSBA GMTs at Day 6 were 289, 3799, 1928, and 1658 for MenQuadfi-primed participants (N=46) and 161, 919, 708, and 800 for MenACWY-CRM-primed participants (N=45) for serogroups A, C, W, and Y, respectively. At D30, the hSBA GMTs were 502, 3708, 2290, and 2308 for MenQuadfi-primed participants (N=174) and 399, 2533, 2574, and 3036 for MenACWY-CRM-primed participants (N=176).

Prior to booster vaccination, the percentage of subjects with hSBA titers ≥1:8 for serogroups A, C, W, and Y were 71.3%, 87.9%, 86.2%, and 79.9% for those who received a prior dose of MenQuadfi 3-6 years earlier (N=174), and 71.0%, 50.6%, 77.8%, and 52.8% for those who received a prior dose of MenACWY-CRM 3-6 years earlier (N=176).

Immunogenicity in Older Adults ≥ 59 Years of Age

Immunogenicity of a dose of MenQuadfi was evaluated in Study 7 (NCT04142242). The study enrolled participants ≥ 59 years of age who had received a prior dose of MenQuadfi or MenACWY-PS at least 3 years previously in Study 4 (NCT02842866).

For a description of study design and number of participants, see Adverse Reactions section Booster Vaccination Following Priming with a Meningococcal Conjugate Vaccine; Vaccination

Following a Prior Dose of a Meningococcal Polysaccharide Vaccine. The primary immunogenicity endpoint was hSBA seroresponse to each serogroup 30 days following vaccination with MenQuadfi in participants who had received a prior dose of MenACWY-PS 3 years previously. Additionally, hSBA seroresponse 30 days following vaccination with MenQuadfi in MenQuadfi-primed participants was also assessed (Table 6). The other endpoints included the hSBA GMTs for each serogroup. These endpoints were also evaluated at 6 days post vaccination in a subset (Per-Protocol Analysis Set 2).

Table 6: Comparison of hSBA Seroresponse Rates 30 Days Following Vaccination with MenQuadfi in Participants ≥ 59 Years of Age Primed with MenQuadfi or Received a Prior Dose of MenACWY-PS At Least 3 Years Previously (Study 7)*

‡Endpoint by Serogroup	MenQuadfi- primed (95% CI)	Prior dose of MenACWY-PS (95% CI)
A	N=145	N=130
% Participants achieving Seroresponse	79.3 (71.8; 85.6)	60.8 (51.8; 69.2)
C		
% Participants achieving Seroresponse	93.1 (87.7; 96.6)	55.0 (46.0; 63.8)
W		
% Participants achieving Seroresponse	90.3 (84.3; 94.6)	49.2 (40.4; 58.1)
Y		
% Participants achieving Seroresponse	92.4 (86.8; 96.2)	49.2 (40.4; 58.1)

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نشرة معتمدة: ...
تاريخ: ٢٠٢٢/٧/٧

* Clinical trial identifier NCT04142242
N: number of subjects in Per-Protocol Analysis Set 1 (D30) with valid serology results.
‡Seroresponse rate (primary endpoint) for each serogroup: the proportion of participants with an hSBA pre vaccination titer < 1:8 who achieved a post-vaccination titer ≥ 1:16, or pre-vaccination titer ≥ 1:8 who achieved a post-vaccination titer at least 4-fold greater than the pre-vaccination titer.
Sufficiency of hSBA seroresponse after MenQuadfi vaccination was demonstrated if the lower limit of the 2-sided 95% CI was >40%.

Seroresponse rates at Day 6 following vaccination with MenQuadfi were 36.2%, 77.6%, 70.7%, and 72.4% for serogroups A, C, W, and Y, respectively, in MenQuadfi-primed participants

(N=58) and 8.1%, 8.1%, 6.5%, and 8.1% for serogroups A, C, W, and Y, respectively, in participants who received a prior dose of MenACWY-PS (N=62). Following vaccination with MenQuadfi, the hSBA GMTs at Day 6 were 44, 206, 118, and 151 for MenQuadfi-primed participants (N=58) and 13, 11, 10, and 11 for participants who received a prior dose of MenACWY-PS (N=62) for serogroups A, C, W, and Y, respectively. At D30, the hSBA GMTs were 162, 638, 419, and 566 for MenQuadfi-primed participants (N=145) and 57, 56, 31, and 41 for participants who received a prior dose of MenACWY-PS (N=130).

Prior to MenQuadfi vaccination, the percentage of subjects with hSBA titers ≥1:8 for serogroups A, C, W, and Y were 64.8%, 73.8%, 66.9%, and 72.4% for those who received a prior dose of MenQuadfi at least 3 years earlier (N=145), and 65.4%, 49.2%, 40.0%, and 41.5% for those who received a prior dose of MenACWY-PS at least 3 years earlier (N=130).

Immunogenicity of Concomitantly Administered Vaccines

Concomitant administration of MenQuadfi with Tdap and HPV in adolescents 10 through 17 years was evaluated in Study 2 (NCT02199691). In this randomized study, 503 participants received MenQuadfi alone, 392 received MenQuadfi coadministered with Tdap and HPV, 296 received Tdap and HPV alone. A fourth group received MenACWY-CRM alone (N=501).

No evidence of interference in hSBA seroresponse rates was observed when MenQuadfi was coadministered with Tdap and HPV. Antibody responses to HPV, and to the tetanus and diphtheria antigens were similar when Tdap and HPV were administered with and without MenQuadfi. Anti-pertussis GMC responses were non-inferior for the pertussis toxoid antigen, but did not meet non-inferiority for the FHA, PRN, and FIM antigens. The clinical relevance of the diminished responses to the pertussis antigens is unknown.

HOW SUPPLIED/STORAGE AND HANDLING

MenQuadfi is supplied in a

- single-dose vial, 0.5 mL in packages of 1 vial

Not all pack sizes may be marketed.

The vial stopper is not made with natural rubber latex.

Store in a refrigerator (2°C – 8°C). Do not freeze. Do not use vaccine that has been frozen. Do not use after expiration date.

Keep out of reach of children.

PATIENT COUNSELING INFORMATION

Prior to administration of MenQuadfi vaccine, the healthcare professional should inform the patient, parent, guardian, or other responsible adult of the potential benefits and risks to the patient [see *Adverse Reactions and Warnings And Precautions*]. Patients, parents, or guardians should be instructed to report any suspected adverse reactions to their healthcare professional who should report these events to Sanofi Pasteur Inc.

MenQuadfi is a registered trademark of Sanofi Pasteur Inc.

Product information as of June 2023

Manufactured by:
Sanofi Pasteur Inc.
Swiftwater PA 18370 USA