Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine Menactra®

For the use of a Registered Medical Practitioner only.

FOR INTRAMUSCULAR INJECTION

INDICATIONS AND USAGE

Menactra®, Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine, is indicated for active immunization to prevent invasive meningococcal disease caused by *N meningitidis* serogroups A, C, Y, and W-135. Menactra is approved for use in individuals 9 months through 55 years of age. Menactra vaccine is not indicated for the prevention of meningitis caused by other microorganisms or for the prevention of invasive meningococcal disease caused by *N meningitidis* serogroup B.

DOSAGE AND ADMINISTRATION

Menactra vaccine is a clear to slightly turbid solution. Parenteral drug products should be inspected visually for container integrity, particulate matter, and discoloration prior to administration, whenever solution and container permit. If any of these conditions exist, the vaccine should not be administered.

Withdraw the 0.5 mL dose of vaccine from the single dose vial using a sterile needle and syringe. Menactra vaccine is administered as a 0.5 mL dose by intramuscular injection. In children 9 through 23 months of age, Menactra vaccine is given as a 2-dose series at least three months apart. Individuals 2 through 55 years of age, Menactra vaccine is given as a single dose.

A single booster dose may be given to individuals 15 through 55 years of age at continued risk for meningococcal disease, if at least 4 to 6 years have elapsed since the prior dose.

Do not administer this product intravenously, subcutaneously, or intradermally.

CONTRAINDICATIONS

Severe allergic reaction (eg, anaphylaxis) after a previous dose of a meningococcal capsular polysaccharide-, diphtheria toxoid- or CRM197-containing vaccine, or to any component of Menactra vaccine (see DESCRIPTION).

WARNINGS AND PRECAUTIONS

Guillain-Barré Syndrome

Persons previously diagnosed with Guillain-Barré Syndrome (GBS) may be at increased risk of GBS following receipt of Menactra vaccine. The decision to give Menactra vaccine should take into account the potential benefits and risks.

GBS has been reported in temporal relationship following administration of Menactra vaccine. The risk of GBS following Menactra vaccination was evaluated in a post-marketing retrospective cohort study (see Post-Marketing Safety Study under Post-marketing Reports).

Preventing and Managing Allergic Vaccine Reactions

Prior to administration, the healthcare provider should review the immunization history for possible vaccine sensitivity and previous vaccination-related adverse reactions to allow an assessment of benefits and risks. Epinephrine and other appropriate agents used for the control of immediate allergic reactions must be immediately available should an acute anaphylactic reaction occur.

Altered Immunocompetence

- *Reduced Immune Response*

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

- *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, Y and W-135, even if they develop antibodies following vaccination with Menactra. [See *Clinical Pharmacology*]

Limitations of Vaccine Effectiveness

Menactra vaccine may not protect all recipients against vaccine serogroups.

Syncope

Syncope (fainting) has been reported following vaccination with Menactra vaccine. Procedures should be in place to prevent falling injury and manage syncopal reactions.

ADVERSE REACTIONS

Clinical Trials Adverse Reactions

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

Children 9 Through 12 Months of Age

The safety of Menactra vaccine was evaluated in four clinical studies that enrolled 3721 participants who received Menactra vaccine at 9 and 12 months of age. At 12 months of age these children also received one or more other recommended vaccines [Measles, Mumps, Rubella and Varicella Virus Vaccine Live (MMRV) or Measles, Mumps, and Rubella Virus Vaccine (MMR) and Varicella Virus Vaccine Live (V) each manufactured by Merck & Co., Inc., Pneumococcal 7-valent Conjugate Vaccine (Diphtheria CRM197 Protein) manufactured by Wyeth Pharmaceuticals Inc. (PCV7), Hepatitis A Vaccine manufactured by Merck & Co., Inc. (HepA). A control group of 997 children was enrolled at 12 months of age and received two or more childhood vaccines [MMRV (or MMR+V), PCV7, HepA] at 12 months of age (see Concomitant Vaccine Administration). Three percent of individuals received MMR and V, instead of MMRV, at 12 months of age.

The primary safety study was a controlled trial that enrolled 1256 children who received Menactra vaccine at 9 and 12 months of age. At 12 months of age these children received MMRV (or MMR+V), PCV7 and HepA. A control group of 522 children received MMRV, PCV7 and HepA. Of the 1778 children, 78% of participants (Menactra vaccine, N=1056; control group, N=322) were enrolled at United States (US) sites and 22% at a Chilean site. (Menactra vaccine, N=200; control group, N=200).

Individuals 2 Through 55 Years of Age

The safety of Menactra vaccine was evaluated in eight clinical studies that enrolled 10,057 participants aged 2–55 years who received Menactra vaccine and 5266 participants who received Menomune – A/C/Y/W-135 vaccine. The three primary safety studies were randomized, active controlled trials that enrolled participants 2–10 years of age (Menactra vaccine, N=1713; Menomune – A/C/Y/W-135 vaccine, N=1519), 11–18 years of age (Menactra vaccine, N=2270; Menomune – A/C/Y/W-135 vaccine, N=972), and 18–55 years of age (Menactra vaccine, N=1384; Menomune – A/C/Y/W-135 vaccine, N=1170), respectively.

As the route of administration differed for the two vaccines (Menactra vaccine given intramuscularly, Menomune – A/C/Y/W-135 vaccine given subcutaneously), study personnel collecting the safety data differed from personnel administering the vaccine.

Booster Vaccination Study

In an open-label trial conducted in the US, 834 individuals were enrolled to receive a single dose of Menactra 4-6 years after a prior dose. The median age of participants was 17.1 years at the time of the booster dose.

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Serious Adverse Events in All Safety Studies
Serious adverse events (SAEs) were reported during a 6-month time period following vaccinations in individuals 9 months through 55 years of age. In children who received Menactra vaccine at 9 months and at 12 months of age, SAEs occurred at a rate of 2.0% - 2.5%. In participants who received one or more childhood vaccine(s) (without co-administration of Menactra vaccine) at 12 months of age, SAEs occurred at a rate of 1.6% - 3.6%, depending on the number and type of vaccines received. In children 2-10 years of age, SAEs occurred at a rate of 0.6% following Menactra vaccine and at a rate of 0.7% following Menomune – A/C/Y/W-135 vaccine. In adolescents 11 through 18 years of age and adults 18 years through 55 years of age, SAEs occurred at a rate of 1.0% following Menactra vaccine and at a rate of 1.3% following Menomune – A/C/Y/W-135 vaccine. In adolescents and adults, SAEs occurred at a rate of 1.3% following booster vaccination with Menactra.

Solicited Adverse Events in the Primary Safety Studies
The most frequently reported solicited injection site and systemic adverse reactions within 7 days following vaccination in children 9 months and 12 months of age were injection site tenderness and irritability. The most frequently reported solicited local and systemic adverse reactions in children aged 2–10 years were injection site pain and irritability. Diarrhea, drowsiness, and anorexia were also common. In adolescents aged 11–18 years and adults aged 18–55 years, the most commonly reported reactions, after a single dose, were injection site pain, headache, and fatigue. Except for redness in adults, injection site reactions were more frequently reported after Menactra vaccination than after Menomune – A/C/Y/W-135 vaccination.

Solicited Adverse Events in a Booster Vaccination Study
For a description of the study design and number of participants, [see *Clinical Trials Experience, Booster Vaccination Study].* The most common solicited injection site and systemic reactions within 7 days of vaccination were pain (60.2%) and myalgia (42.8%), respectively. Overall rates of solicited injection site reactions and solicited systemic reactions were similar to those observed in adolescents and adults after a single Menactra dose. The majority of solicited reactions were Grade 1 or 2 and resolved within 3 days.

Adverse Events in Concomitant Vaccine Studies
Solicited Injection Site and Systemic Reactions when Given with Routine Pediatric Vaccines
For a description of the study design and number of participants [see *Clinical Trials Experience, Concomitant Vaccine Administration*]. In the primary safety study, 1378 US children were enrolled to receive Menactra vaccine alone at 9 months of age and Menactra vaccine plus one or more other routinely administered vaccines (MMRV, PCV7 and HepA) at 12 months of age (N=961). Another group of children received two or more routinely administered vaccines (MMRV, PCV7 and HepA) (control group, n=321) at 12 months of age. Participants who received Menactra vaccine and the concomitant vaccines at 12 months of age described above reported similar frequencies of tenderness, redness and swelling at the Menactra vaccine injection site and at the concomitant vaccine injection sites. Tenderness was the most frequent injection site reaction (48%, 39%, 46% and 43% at the Menactra vaccine, MMRV, PCV7 and HepA sites, respectively). Irritability was the most frequent systemic reaction, reported in 62% of recipients of Menactra vaccine plus concomitant vaccines, and 65% of the control group. (See Concomitant Vaccine Administration).

Solicited Injection Site and Systemic Reactions When Given With Tetanus and Diphtheria Toxoid Adsorbed Vaccine (Td)
Injection site pain was reported more frequently after Td vaccination than after Menactra vaccination (71% versus 53%). The overall rate of systemic adverse events was higher when Menactra and Td vaccines were given concomitantly than when Menactra vaccine was administered 28 days after Td (59% versus 36%). In both groups, the most common reactions were headache (Menactra vaccine + Td, 36%; Td + Placebo, 34%; Menactra vaccine alone, 22%) and fatigue (Menactra vaccine + Td, 32%; Td + Placebo, 29%; Menactra vaccine alone, 17%).
Fever ≥40.0ºC occurred at ≤0.5% in all groups.

Solicited Injection Site and Systemic Reactions When Given With Typhoid Vi Polysaccharide Vaccine
More participants experienced pain after Typhoid vaccination than after Menactra vaccination (Typhoid + Placebo, 76% versus Menactra vaccine + Typhoid, 47%). The majority (70%-77%) of injection site solicited reactions for both groups at either injection site were reported as Grade 1 and resolved within 3 days post-vaccination. In both groups, the most common systemic reaction was headache (Menactra vaccine + Typhoid, 41%; Typhoid + Placebo, 42%; Menactra vaccine alone, 33%) and fatigue (Menactra vaccine + Typhoid, 38%;

Typhoid + Placebo, 35%; Menactra vaccine alone, 27%). Fever ≥40.0ºC and seizures were not reported in either group.

Post-Marketing Reports
In addition to reports in clinical trials, worldwide voluntary adverse events reports received since market introduction of Menactra vaccine are listed below. This list includes serious events and/or events which were included based on severity, frequency of reporting or a plausible causal connection to Menactra vaccine. Because these events were reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or to establish a causal relationship to vaccination.

- *Blood & Lymphatic System Disorders*
  Lymphadenopathy
- *Immune system disorders*
  Hypersensitivity reactions such as anaphylaxis/anaphylactic reaction, wheezing, difficulty breathing, upper airway swelling, urticaria, erythema, pruritus, hypotension.
- *Nervous system disorders*
  Guillain-Barré syndrome, paraesthesia, vasovagal syncope, dizziness, convulsion, facial palsy, acute disseminated encephalomyelitis, transverse myelitis
- *Musculoskeletal and connective tissue disorders*
  Myalgia
- *General disorders and administrative site conditions*
  Large injection site reactions, extensive swelling of the injected limb (may be associated with erythema, warmth, tenderness or pain at the injection site).

Post-marketing Safety Study
The risk of GBS following receipt of Menactra vaccine was evaluated in a US retrospective cohort study using healthcare claims data from 9,578,688 individuals 11 through 18 years of age, of whom 1,431,906 (15%) received Menactra vaccine. Of 72 medical chart confirmed GBS cases, none had received Menactra vaccine within 42 days prior to symptom onset. An additional 129 potential cases of GBS could not be confirmed or excluded due to absent or insufficient medical chart information. In an analysis that took into account the missing data, estimates of the attributable risk of GBS ranged from 0 to 5 additional cases of GBS per 1,000,000 vaccinees within the 6 week period following vaccination.

DRUG INTERACTIONS
Concomitant Administration with Other Vaccines
Menactra vaccine was concomitantly administered with Typhim Vi® [Typhoid Vi Polysaccharide Vaccine] (Typhoid) and Tetanus and Diphtheria Toxoids Adsorbed, For Adult Use (Td), in individuals 18 through 55 and 11 through 17 years of age, respectively (see CLINICAL STUDIES and ADVERSE REACTIONS).

In children younger than 2 years of age, Menactra was co-administered with one or more of the following vaccines: PCV7, MMR, V, MMRV, or HepA (see Clinical Studies and Adverse Reactions).

Data are not available to assess the safety and immunogenicity of Menactra and DTaPcontaining vaccines when administered concomitantly at 15 months of age.

Pneumococcal antibody responses to some serotypes in PCV7 were decreased following coadministration of Menactra vaccine and PCV7 (see Concomitant Vaccine Administration).
Do not mix Menactra vaccine with other vaccines in the same syringe. When Menactra vaccine is administered concomitantly with other injectable vaccines, the vaccines should be administered with different syringes and given at separate injection sites.

Immunosuppressive Therapies
Immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs, and corticosteroids (used in greater than physiologic doses) may reduce the immune response to vaccines.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. There are no adequate and well-controlled studies of Menactra administration in pregnant women in the US. Available data suggest that rates of major birth defects and miscarriage in women who received Menactra 30 days prior to pregnancy or during pregnancy are consistent with estimated background rates.

A developmental toxicity study was performed in female mice given 0.1 mL (in divided doses) of Menactra prior to mating and during gestation (a single human dose is 0.5 mL). The study revealed no evidence of harm to the fetus due to Menactra.

Data

Human Data

A pregnancy registry spanning 11 years (2005-2016) included 222 reports of exposure to Menactra from 30 days before or at any time during pregnancy. Of these reports, 87 had known pregnancy outcomes available and were enrolled in the pregnancy registry prior to the outcomes being known. Outcomes among these prospectively followed pregnancies included 2 major birth defects and 6 miscarriages.

Animal Data

A developmental toxicity study was performed in female mice. The animals were administered 0.1 mL of Menactra (in divided doses) at each of the following time points: 14 days prior to mating, and on Days 6 and 18 of gestation (a single human dose is 0.5 mL). There were no vaccine-related fetal malformations or variations, and no adverse effects on pre-weaning development observed in the study.

Lactation

Risk Summary

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Menactra and any potential adverse effects on the breastfed child from Menactra. Data are not available to assess the effects of Menactra on the breastfed infant or on milk production/excretion.

Pediatric Use

Menactra is not approved for use in infants under 9 months of age. Available data show that infants administered three doses of Menactra (at 2, 4, and 6 months of age) had diminished responses to each meningococcal vaccine serogroup compared to older children given two doses at 9 and 12 months of age

Geriatric Use

Safety and effectiveness of Menactra vaccine in adults older than 55 years have not been established.

DESCRIPTION

Menactra vaccine is a sterile, intramuscularly administered vaccine that contains Neisseria meningitidis serogroup A, C, Y, and W-135 capsular polysaccharide antigens individually conjugated to diphtheria toxoid protein. N meningitidis A, C, Y, and W-135 strains are cultured on Mueller Hinton casein agar and grown in Watson Scherp casamino acid media. 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, they are depolymerized, derivatized, and purified by diafiltration. Corynebacterium diphtheriae cultures are grown in a modified Mueller and Miller casein medium and detoxified with formaldehyde. The diphtheria toxoid protein is purified by ammonium sulfate fractionation and diafiltration. The derivatized polysaccharides are covalently linked to diphtheria toxoid and purified by serial diafiltration. The four meningococcal components, present as individual serogroup-specific glycoconjugates, compose the final formulated vaccine. No preservative or adjuvant is added during manufacture. Each 0.5 mL dose may contain residual amounts of formaldehyde of less than 2.66 mcg (0.000532%), by calculation. Potency of Menactra vaccine is determined by quantifying the amount of each polysaccharide antigen that is conjugated to diphtheria toxoid protein and the amount of unconjugated polysaccharide present. Menactra vaccine is manufactured as a sterile, clear to slightly turbid liquid. Each 0.5 mL dose of vaccine is formulated in sodium phosphate buffered

isotonic sodium chloride solution to contain 4 mcg each of meningococcal A, C, Y, and W-135 polysaccharides conjugated to approximately 48 mcg of diphtheria toxoid protein carrier.

The vial stopper is not made with natural rubber latex.

CLINICAL PHARMACOLOGY

Mechanism of Action

The presence of bactericidal anti-capsular meningococcal antibodies has been associated with protection from invasive meningococcal disease. Menactra vaccine induces the production of bactericidal antibodies specific to the capsular polysaccharides of serogroups A, C, Y, and W-135.

NON-CLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility

Menactra vaccine has not been evaluated for carcinogenic or mutagenic potential or for impairment of male fertility. A developmental animal toxicity study showed that Menactra had no effects on female fertility in mice [see Pregnancy]

CLINICAL STUDIES

Efficacy

The Serum Bactericidal Assay (SBA) used to test sera contained an exogenous complement source that was either human (SBA-H) or baby rabbit (SBA-BR). The response to vaccination following two doses of vaccine administered to children 9 and 12 months of age and following one dose of vaccine administered to children 2 through 10 years of age was evaluated by the proportion of subjects having an SBA-H antibody titer of 1:8 or greater, for each serogroup. In individuals 11 through 55 years of age, the response to Menactra vaccination was evaluated by the proportion of subjects with a 4-fold or greater increase in baseline bactericidal antibody to each serogroup as measured by SBA-BR. For individuals 2 through 55 years of age, vaccine efficacy was inferred from the demonstration of immunologic equivalence to a US-licensed meningococcal polysaccharide vaccine, Menomune – A/C/Y/W-135 vaccine as assessed by Serum Bactericidal Assay (SBA)

Immunogenicity

Children 9 through 12 Months of Age

In a randomized, US, multi-center trial, children received Menactra vaccine at 9 months and 12 months of age. The first Menactra dose was administered alone, followed by a second Menactra vaccine dose given alone (N=404), or with MMRV (N=302), or with PCV7 (N=422). For all participants, sera were obtained approximately 30 days after last vaccination. There were no substantive differences in demographic characteristics between the vaccine groups. The median age range for administration of the first dose of Menactra was 278-279 days of age. Administration of Menactra to children at 12 months and 15 months of age was evaluated in a US study. Prior to the first dose, 33.3% [n=16/48] of participants had an SBA-H titer $\geq$1:8 to Serogroup A, and 0-2% [n=0-1 of 50-51] to Serogroups C, Y and W-135. After the second dose, percentages of participants with an SBA-H titer $\geq$1:8 were: 85.2%, Serogroup A [n=46/54]; 100.0%, Serogroup C [n=54/54]; 96.3%, Serogroup Y [n=52/54]; 96.2%, Serogroup W-135 [n=50/52].

Individuals 2 through 55 Years of Age

Immunogenicity was evaluated in three comparative, randomized, US, multi-center, active controlled clinical trials that enrolled children (2 through 10 years of age), adolescents (11 through 18 years of age), and adults (18 through 55 years of age). Participants received a single dose of Menactra vaccine (N=2526) or Menomune – A/C/Y/W-135 vaccine (N=2317). For all age groups studied, sera were obtained before and approximately 28 days after vaccination. (Blinding procedures for safety assessments are described in Adverse Reactions.) In each of the trials, there were no substantive differences in demographic characteristics between the vaccine groups, between immunogenicity subsets or the overall study population.

Immunogenicity in Children 2 through 10 Years of Age

Of 1408 enrolled children 2 through 10 years of age, immune responses evaluated by SBA-H in a subset of Menactra vaccine participants (2 through 3 years of age, N=52; 4 through 10 years of age, N=84) and Menomune – A/C/Y/W-135 vaccine participants (2 through 3 years of age, N=53;4 through 10 years of age, N=84), the percentages of subjects with a titer $\geq$1:8 were consistently higher in the Menactra group for all four serogroups.

In the evaluated subset of participants 2 through 3 years of age, the percentage of participants with an SBA-H titer ≥1:8 at Day 28 were 73%, Serogroup A; 63%, Serogroup C; 88%, Serogroup Y; 63%, Serogroup W-135 in the Menactra group and 64%, Serogroup A; 38%, Serogroup C; 73%, Serogroup Y; and 33%, Serogroup W-135 in the Menomune group.

In the subset of participants 2 through 3 years of age with undetectable pre-vaccination titers (ie, SBA-H titers <1:4 at Day 0), seroconversion rates (defined as the proportions of participants with SBA-H titers ≥1:8 by Day 28) were similar between the Menactra and Menomune – A/C/Y/W-135 recipients. Menactra participants achieved seroconversion rates of: 57%, Serogroup A (n=12/21); 62%, Serogroup C (n=29/47); 84%, Serogroup Y (n=26/31); 53%, Serogroup W-135 (n=20/38). The seroconversion rates for Menomune – A/C/Y/W-135 recipients were: 55%, Serogroup A (n=16/29); 30%, Serogroup C (n=13/43); 57%, Serogroup Y (n=17/30); 26%, Serogroup W-135 (n=11/43).

In the evaluated subset of participants 4 through 10 years of age, the percentage of participants with an SBA-H titer ≥1:8 at Day 28 were 81%, Serogroup A; 79% Serogroup C; 99%, Serogroup Y; 85%, Serogroup W-135 in the Menactra group and 55%, Serogroup A; 48%, Serogroup C; 92%,Serogroup Y; and 79%, Serogroup W-135 in the Menomune group.

In the subset of participants 4 through 10 years of age with undetectable pre-vaccination titers (ie, SBA-H titers <1:4 at Day 0), seroconversion rates (defined as the proportions of participants with SBA-H titers ≥1:8 by Day 28) were similar between the Menactra and Menomune – A/C/Y/W-135 recipients. Menactra participants achieved seroconversion rates of: 69%, Serogroup A (n=11/16); 81%, Serogroup C (n=50/62); 98%, Serogroup Y (n=45/46); 69%, Serogroup W-135 (n=27/39). The seroconversion rates for Menomune – A/C/Y/W-135 recipients were: 48%, Serogroup A (n=10/21); 38%, Serogroup C (n=19/50); 84%, Serogroup Y (n=38/45); 68%, Serogroup W-135 (n=26/38).

Immunogenicity in Adolescents 11 through 18 Years of Age
Results from the comparative clinical trial conducted in 881 adolescents (aged 11 through 18 years) showed that the immune responses measured by SBA-BR to Menactra vaccine and Menomune – A/C/Y/W-135 vaccine were similar for all four serogroups. The percentage of participants with an SBA-BR titer with a ≥ 4-fold rise from the baseline were 93%, Serogroup A; 92%, Serogroup C; 82%, Serogroup Y; 97%, Serogroup W-135 in the Menactra group and 92%, Serogroup A; 89%, Serogroup C; 80%, Serogroup Y; and 95%, Serogroup W-135 in the Menomune group. In participants with undetectable pre-vaccination titers (ie, less than 1:8 at Day 0), seroconversion rates (defined as a ≥4-fold rise in Day 28 SBA-BR titers) were similar between the Menactra vaccine and Menomune – A/C/Y/W-135 vaccine recipients. Menactra vaccine participants achieved seroconversion rates of: 100%, Serogroup A; 99%, Serogroup C; 98%, Serogroup Y; and 98%, Serogroup W-135. The seroconversion rates for Menomune – A/C/Y/W-135 vaccine recipients were: 100%, Serogroup A; 99%, Serogroup C; 100%, Serogroup Y; 99%, Serogroup W-135.

Immunogenicity in Adults 18 through 55 Years of Age
Results from the comparative clinical trial conducted in 2554 adults aged 18 through 55 years showed that the immune responses measured by SBA-BR to Menactra vaccine and Menomune – A/C/Y/W-135 vaccine were similar for all four serogroups. The percentage of participants with an SBA-BR titer with a ≥4-fold rise from the baseline were 81%, Serogroup A; 89%, Serogroup C; 74%, Serogroup Y; and 89%, Serogroup W-135 in the Menactra group and 85%, Serogroup A; 90%, Serogroup C; 79%, Serogroup Y; and 94%, Serogroup W-135 in the Menomune group.

In participants with undetectable pre-vaccination titers (ie, less than 1:8 at Day 0), seroconversion rates (defined as a ≥4-fold rise in Day 28 SBA-BR titers) were similar between the Menactra vaccine and Menomune – A/C/Y/W-135 vaccine recipients. Menactra vaccine participants achieved seroconversion rates of: 100%, Serogroup A; 99%, Serogroup C; 91%, Serogroup Y; and 97%, Serogroup W-135. The seroconversion rates for Menomune – A/C/Y/W-135 vaccine recipients were: 99%, Serogroup A; 98%, Serogroup C; 97%, Serogroup Y; and 99%, Serogroup W-135.

Immunogenicity in Adolescents and Adults Following Booster Vaccination
For a description of the study design and number of participants, [see Clinical Trials Experience, Booster Vaccination Study] Prior to revaccination, the percentage of participants (n=781) with an SBA-H titer ≥1:8 were 64.5%, 44.2%, 38.7%, and 68.5% for Serogroups A, C, Y, and W- 135, respectively. Among the subset of trial participants (n=112) for whom SBA-H responses at Day 6 were assessed, 86.6%, 91.1%, 94.6%, and 92.0% achieved a ≥4-fold rise in SBA-H titer for Serogroups A, C, Y, and W-135, respectively. The proportions of participants (n=781) who achieved a ≥4-fold rise in SBA-H titer by Day 28 were 95.0%, 95.3%, 97.1%, and 96% for Serogroups A, C, Y, and W-135, respectively. The proportions of participants who achieved an SBA-H titer ≥1:8 by Day 28 were >99% for each serogroup.

Concomitant Vaccine Administration
MMRV (or MMR+V) or PCV7
In a US, active-controlled trial, 1179 children received Menactra vaccine at 9 months and 12 months of age. At 12 months of age these children received Menactra concomitantly with MMRV (N=616), or MMR+V (N=48), or PCV7 (N=250). Another group of 12-month old children received MMRV+PCV7 (N=485). Sera were obtained approximately 30 days after the last vaccinations. Measles, mumps, rubella and varicella antibody responses among children who received Menactra vaccine and MMRV (or MMR and V) were comparable to corresponding antibody responses among children who received MMRV and PCV7. When Menactra was given concomitantly with PCV7, the non-inferiority criteria for comparisons of pneumococcal IgG GMCs (upper limit of the two-sided 95% CI of the GMC ratio ≤2) were not met for 3 of 7 serotypes (4, 6B, 18C). In a subset of subjects with available sera, pneumococcal opsonophagocytic assay GMT data were consistent with IgG GMC data.

Td
In a double-blind, randomized, controlled trial, 1021 participants aged 11 through 17 years received Td and Menactra vaccines concomitantly (N=509), or Td followed one month later by Menactra vaccine (N=512). Sera were obtained approximately 28 days after each respective vaccination. The proportion of participants with a 4-fold or greater increase in SBA-BR titer to meningococcal Serogroups C, Y and W-135 was higher when Menactra vaccine was given concomitantly with Td (86-96%) than when Menactra vaccine was given one month following Td (65-91%). Anti-tetanus and anti-diphtheria antibody responses were similar in both study groups.

Typhim Vi (Typhoid Vi Polysaccharide Vaccine)
In a double-blind, randomized, controlled trial, 945 participants aged 18 through 55 years received Typhim Vi and Menactra vaccines concomitantly (N=469), or Typhim Vi vaccine followed one month later by Menactra vaccine (N=476). Sera were obtained approximately 28 days after each respective vaccination. The antibody responses to Menactra vaccine and to Typhim Vi vaccine components were similar in both study groups.

HOW SUPPLIED
Vial, 1 Dose (1 vial per package).

STORAGE
Store at 2° to 8°C (35° to 46°F). DO NOT FREEZE. Product that has been exposed to freezing should not be used. Do not use after expiration date.

Shelf life of the product is 24 months when stored at 2°C to 8°C.

Manufactured by:
Sanofi Pasteur Inc.
Swiftwater PA 18370 USA

Imported and Marketed by:
Sanofi Pasteur India Private Limited
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INFORMATION FOR PATIENTS

Prior to administration of Menactra 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 India Private Limited.

Updated: Sep 2019

Source: 1) US PI, v0.4 dated 26th April 2018
2) CCDS v14 dated 23rd May 2017

Registered Medical Practitioners can refer to the company website http://www.sanofi.in for the latest prescribing information