Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT

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

Brand Name: Menactra®

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Component	**Formulated Concentration Quantity/0.5 mL Dose**	**Function**
Meningococcal (Serogroup A) Polysaccharide (Monovalent Conjugate)	4 µg	Active ingredient
Meningococcal (Serogroup C) Polysaccharide (Monovalent Conjugate)	4 µg	Active ingredient
Meningococcal (Serogroup Y) Polysaccharide (Monovalent Conjugate)	4 µg	Active ingredient
Meningococcal (Serogroup W-135) Polysaccharide (Monovalent Conjugate)	4 µg	Active ingredient
Diphtheria Toxoid Protein	48 µg*	Carrier protein for all serogroup polysaccharide conjugate
Sodium Chloride	4.35 mg	Excipient used to create an isotonic solution (Inactive ingredient)
Sodium Phosphate	0.7 mg	Excipient used to maintain pH (Inactive ingredient)

* Diphtheria Toxoid quantity is approximate and dependent on the conjugate polysaccharide to protein ratio

3. PHARMACEUTICAL FORM

Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine, for intramuscular use, is presented in one dosage form. This dosage form is a **sterile, aqueous solution** that contains group-specific polysaccharide antigens from *Neisseria meningitidis* Serogroup A, Serogroup C, Serogroup Y, and Serogroup W- 135 separately conjugated to Diphtheria Toxoid protein. Each 0.5 mL dose is formulated to contain 4 µg of each meningococcal A, C, Y, and W-135 polysaccharides conjugated to a total of approximately 48 µg of Diphtheria Toxoid protein carrier.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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 2 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.

4.2 Posology and method of 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 should be administered as a single 0.5 mL injection by the **intramuscular** route, preferably in the deltoid region.

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

The need for, or timing of, a booster dose of Menactra vaccine has not yet been determined.

4.3 Contraindications

Severe allergic reaction (eg, anaphylaxis) after a previous dose of a meningococcal capsular polysaccharide-, diphtheria toxoid- or CRM_{197}-containing vaccine, or to any component of Menactra vaccine.

4.4 Special warnings and precautions for use

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

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to Menactra vaccine.

Limitations of Vaccine Effectiveness

Menactra vaccine may not protect all recipients against vaccine serogroups.

4.5 Interaction with other medicinal products and other forms of interaction

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 Pharmacodynamic properties and Undesirable effects).

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.

4.6 Pregnancy and lactation

Animal reproduction studies have not demonstrated a risk with respect to effects on pregnancy and embryo-fetal development, parturition, and postnatal development. However, since there are no adequate and well controlled studies in pregnant women,

Menactra vaccine should be given to a pregnant woman only if clearly needed (such as during an outbreak or prior to necessary travel to an endemic area) and only following an assessment involving the healthcare professional and patient of the risks and benefits.

Considering the severity of the meningococcal disease, pregnancy should not preclude vaccination when the risk is clearly identified.

Nursing Mothers

It is not known whether Menactra vaccine is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Menactra vaccine is administered to a nursing woman.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects

Clinical Trial 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.

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.

Serious Adverse Events in All Safety Studies

Serious adverse events (SAEs) were reported during a 6-month time period following vaccinations in individuals 2 through 55 years of age. 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 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.

Solicited Adverse Events in the Primary Safety Studies

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 ages 11–18 years and adults ages 18–55 years, the most commonly reported reactions 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.

Adverse Events in Concomitant Vaccine Studies

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.

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 – MyalgiaPost-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.

4.9 Overdose

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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 Menactra vaccination 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
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 ≥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 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.

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 99%, 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.

ATC code: J07AH

- *J : Anti-infectives for systemic use*
- *J07 : Vaccines*
- *J07A : Bacterial*

vaccines J07AH :
Meningococcal vaccine

5.2 Pharmacokinetic properties
No pharmacokinetic studies have been performed.

5.3 Preclinical safety data
Carcinogenesis, Mutagenesis, Impairment of Fertility
Menactra vaccine has not been evaluated for carcinogenic or mutagenic potential or for impairment of fertility.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Chloride, USP (within 0.85% Physiological Saline and 0.5 M Phosphate Buffered Saline, pH 6.8)	4.35 mg	Excipient used to create an isotonic solution (Inactive ingredient)
Sodium Phosphate, Dibasic, Anhydrous (within 0.5 M Phosphate Buffered Saline, pH 6.8)	0.348 mg	Excipient used to maintain pH (Inactive ingredient)
Sodium Phosphate, Monobasic, Monohydrate,	0.352 mg	Excipient used to maintain pH
Crystal, USP		(Inactive ingredient)
(within 0.5 M Phosphate Buffered Saline,		
pH 6.8)		

6.2 Incompatibilities
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.

6.3 Shelf life
24 months at 2-8 ºC

6.4 Special precautions for 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.

6.5 Nature and contents of container
The vaccine is manufactured as a single dose unit, containing 0.5 mL of solution.

Containers and devices	**Container element**	**Nature**
Single dose vial	Vial Vial Stopper Seal *fitted with a flip off button*	Type I borosilicate glass Chlorobutyl synthetic polyisoprene blend Crimped aluminum cap (11)
Single dose syringe *(Without needle)*	*Barrel* *Plunger* *Plunger rod* *Tip cap*	*Type I borosilicate glass* *bromobutyl (latex-free) rubber stopper compound siliconized with dimethicone* *Polystyrene* *FM27 rubber compound* (12)

6.6 Special precautions for disposal
After use, any remaining vaccine and container must be disposed of safely, preferably by heat inactivation or incineration, according to locally agreed procedures.

7. MARKET AUTHORIZATION HOLDER

Sanofi Pasteur India Private Limited
54/A, M. Vasanji Road,
Andheri (East)
Mumbai 400 093