PRODUCT MONOGRAPH

MENOMUNE® - A/C/Y/W-135

Meningococcal Polysaccharide Vaccine,

Groups A, C, Y and W-135 Combined

Powder for Solution

Active Immunizing Agent for the Prevention of Meningococcal Meningitis

ATC Code: J07AH

Manufactured by:
Sanofi Pasteur Inc.
Swiftwater, PA 18370 USA

Distributed by:
Sanofi Pasteur Limited
Toronto, Ontario, Canada

Control No.: 151001 **Date of Approval: July 30, 2013**

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PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration

Subcutaneous injection

Dosage Form / Strength

Powder for solution

Each 0.5 mL dose is formulated to contain:

Active Ingredients

50 µg of each *Neisseria meningitidis* group-specific polysaccharide antigen (A, C, Y and W-135)

Clinically Relevant Non-Medicinal Ingredients

N/A

For a complete listing see DOSAGE FORMS, COMPOSITION AND PACKAGING

DESCRIPTION

MENOMUNE® - A/C/Y/W-135 [Meningococcal Polysaccharide Vaccine, Groups A, C, Y and W-135 Combined] is a freeze-dried preparation of the Group-specific polysaccharide antigens from *Neisseria meningitidis*, Group A, Group C, Group Y, and Group W-135. After reconstitution with diluent, the vaccine is a clear colourless liquid.

INDICATIONS AND CLINICAL USE

MENOMUNE® - A/C/Y/W-135 is indicated for active immunization against invasive meningococcal disease caused by *Neisseria meningitidis*, serogroups A, C, Y and W-135, in persons 2 years of age and older.

It will not protect against other etiologic agents, including *N. meningitidis* Group B, that cause meningococcal disease or non-meningococcal meningitis.

MENOMUNE® - A/C/Y/W-135 is not indicated for infants and children younger than 2 years of age, except as recommended by the National Advisory Committee on Immunization (NACI) for the protection of infants 3 months and older for control of outbreaks of serogroup A meningococcal disease (1) (see DOSAGE AND ADMINISTRATION).

MENOMUNE® - A/C/Y/W-135 is recommended by NACI (National Advisory Committee on Immunization) for certain groups with increased risk of the disease such as individuals with functional or anatomic asplenia, persons with complement, properdin or factor D deficiency, military recruits and travellers to high risk areas, and research, industrial and clinical laboratory personnel who are routinely exposed to *N. meningitidis* cultures. (2)

Outbreak control

MENOMUNE® - A/C/Y/W-135 is recommended by NACI for outbreak management of meningococcal disease (see DOSAGE AND ADMINISTRATION). (2)

CONTRAINDICATIONS

Hypersensitivity

Known systemic hypersensitivity to any component of MENOMUNE® - A/C/Y/W-135, the container or after a previous dose of MENOMUNE® - A/C/Y/W-135 or a vaccine containing the same components are contraindications to vaccination. (See components listed in DOSAGE FORMS, COMPOSITION AND PACKAGING.)

WARNINGS AND PRECAUTIONS

General

Before administration of MENOMUNE® - A/C/Y/W-135,health-care providers should inform the recipient or the parent or guardian of the recipient of the benefits and risks of immunization, inquire about the recent health status of the recipient, review the recipient's history concerning possible hypersensitivity to the vaccine or similar vaccines, previous immunization history, the presence of any contraindications to immunization and comply with any local requirements regarding information to be provided to the recipient/guardian before immunization.

It is extremely important that the recipient, parent or guardian be questioned concerning any signs or symptoms of an adverse reaction after a previous dose of vaccine containing similar components. (See CONTRAINDICATIONS and ADVERSE REACTIONS.)

Protection

MENOMUNE® - A/C/Y/W-135 will not stimulate protection against infections caused by organisms other than Groups A, C, Y and W-135 meningococci. As with any vaccine, immunization with MENOMUNE® - A/C/Y/W-135 may not protect 100% of vaccinated individuals.

Administration Route Related Precautions:

Do not administer MENOMUNE® - A/C/Y/W-135 by intravascular injection: ensure that the needle does not penetrate a blood vessel. Special care should be taken to avoid injecting the vaccine intradermally or intramuscularly. A separate sterile needle and syringe, or a sterile disposable unit should be used for each individual recipient to prevent disease transmission (see DOSAGE AND ADMINISTRATION).

Febrile and Acute Disease:

Vaccination should be postponed in cases of an acute or febrile illness. (3) However, an illness with a low-grade fever should not usually be a reason to postpone vaccination.

Immune

Individuals with functional or anatomical asplenia may produce an immune response to MENOMUNE® - A/C/Y/W-135, however, the degree of protection that would be afforded is unknown. (4)

If MENOMUNE® - A/C/Y/W-135 is administered to persons with congenital or acquired immune deficiency or to persons receiving immunosuppressive therapy, an adequate immunologic response may not be obtained. If possible, consideration should be given to delaying vaccination until after the completion of any immunosuppressive treatment. Nevertheless, vaccination of persons with chronic immunodeficiency such as HIV infection is recommended even if the immune response might be limited. (3) (5)

The possibility of allergic reactions in persons sensitive to components of the vaccine should be evaluated.

As the stopper of the vial for this product contains dry natural latex rubber caution should be exercised when the vaccine is administered to subjects with known hypersensitivity to latex. The diluent for the multidose vial contains Thimerosal as a preservative. For individuals sensitive to Thimerosal, the single-dose presentation should be used.

As with all products, epinephrine hydrochloride solution (1:1,000) and other appropriate agents should be available for immediate use in case an anaphylactic or acute hypersensitivity reaction occurs. Health-care providers should be familiar with current recommendations for the initial management of anaphylaxis in non-hospital settings, including proper airway management (5) (6) For instructions on recognition and treatment of anaphylactic reactions, see the current edition of the Canadian Immunization Guide or visit the Health Canada website.(5)

Peri-Operative Considerations

The National Advisory Committee on Immunization (NACI) states that if possible, MENOMUNE® - A/C/Y/W-135 and other indicated vaccines should be given 2 weeks before splenectomy.

Special Populations

Pregnant Women

Animal reproduction studies have not been conducted with MENOMUNE® - A/C/Y/W-135. It is also not known whether MENOMUNE® - A/C/Y/W-135 can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity.

MENOMUNE® - A/C/Y/W-135 should be given to a pregnant woman only if clearly needed and the expected benefit outweighs any potential risk. Limited data to date have found no evidence of teratogenicity of the polysaccharide quadrivalent meningococcal vaccine when given to pregnant women. (7) (8)

Nursing Women

It is not known whether this vaccine is excreted in human milk. Caution must be exercised when MENOMUNE® - A/C/Y/W-135 is administered to a nursing mother.

Pediatrics

Safety and effectiveness of MENOMUNE® - A/C/Y/W-135 in children below the age of 2 years have not been established. MENOMUNE® - A/C/Y/W-135 is not indicated for infants and children younger than 2 years of age except as recommended by NACI for the protection of infants 3 months and older for control of outbreaks of serogroup A meningococcal disease. (1) (See INDICATIONS AND CLINICAL USE).

ADVERSE REACTIONS

Clinical Trial Adverse Drug 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 rates observed in practice. The adverse reaction information from clinical trials does, however, provide a basis for identifying the adverse events that appear to be related to vaccine use and for approximating rates of those events.

Controlled clinical trials to assess the safety and immunogenicity of another vaccine, Menactra® [Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine], were conducted in which participants were randomized to receive Menactra® or MENOMUNE® - A/C/Y/W-135 used as a control vaccine.

Two randomized, active-controlled primary safety studies were conducted using MENOMUNE® - A/C/Y/W-135 as a control arm, in 2,221 children aged 2 to 10 years who had never received any meningococcal vaccination previously. (9) (10)

Participants were monitored daily for solicited injection site and systemic reactions for 7-days post-vaccination. Participants were monitored for 28 days for unsolicited adverse events and for 6 months post-vaccination for serious adverse events.

The most commonly reported solicited reactions were injection site pain, irritability, drowsiness, anorexia and diarrhea. (See Table 1). The majority of the solicited injection site and systemic reactions reported within 7 days after vaccination were mild, with a mean duration of no more than 2 days for the local reactions and less than 4 days for the systemic reactions.

Table 1: Percentage of Children 2-10 Years of Age Reporting at Least One Solicited Reaction Within 7 Days Following Administration of MENOMUNE® - A/C/Y/W-135, by Study (9) (10)

Event	Study 603-02 Menomune®-A/C/Y/W-135 N = 692		Study MTA08 Menomune®-A/C/Y/W-135 N = 1,515	
	Any*	Severe†	Any	Severe
Injection Site Reactions				
Pain	46.9	0.3	30.4	0.0
Redness	30.4	0.4	9.4	0.0
Induration	15.6	0.1	5.2	0.0
Swelling	14.6	0.3	4.9	0.0
Systemic Reactions				
Irritability‡	30.1	0.6	12.1	0.4
Drowsiness‡	24.1	1.1	10.9	0.3
Anorexia§	20.3	0.4	9.2	0.7
Diarrhea**	15.7	0.4	13.0	0.3
Fever††	12.0	0.6	6.0	0.3
Vomiting‡‡	7.0	1.1	3.1	0.4
Hives§§	0.4	-	-	-
Arthralgia‡	-	-	7.6	0.0
Rash§§	-	-	3.5	-
Seizures§§	-	-	0.0	-

* Any denotes the proportion of participants reporting any reaction regardless of the severity

† Severe local reactions denotes swelling, redness, or induration ≥ 2.0 inches n diameter or pain resulting in unwillingness to move the affected arm.

‡ Severe: requiring bed rest

§ Severe: skipped ≥ 3 meals

** Severe: ≥ 5 episodes

†† Severe: ≥ 39.5°C

‡‡ Severe: ≥ 3 episodes

§§ These solicited adverse events were reported as present or absent only.

Four clinical studies conducted similarly, enrolled adolescents 11-18 years of age (Trial MTA02 and Trial MTA04), and adults 18 - 55 years of age (Trial MTA09 and MTA14), respectively. (11) (12) (13)

Participants were monitored daily for 7-days post-vaccination, for solicited injection site and systemic reactions. Safety data were collected from participants for 28 days for unsolicited adverse events and for 6 months post-vaccination for visits to an emergency room, unexpected visits to an office physician, and serious adverse events.

The most commonly reported solicited adverse reactions in adolescents, ages 11 - 18 years, and adults, ages 18 - 55 years, were injection site pain, headache and fatigue. (See Table 2). The majority of the solicited injection site and systemic reactions following MENOMUNE® - A/C/Y/W-135 vaccination were reported as mild in intensity, with a mean duration of no more than 2 days for any injection site reaction and less than 4 days for any systemic reaction.

Table 2: Percentage of Individuals Reporting at Least One Solicited Reaction Within 7 days Following Administration of MENOMUNE® - A/C/Y/W-135, by Age Category (11) (12) (13)

Event	Menomune®-A/C/Y/W-135 Adolescents N = 1,411*		Menomune®-A/C/Y/W-135 Adults N = 1,613†	
	Any‡	Severe§	Any	Severe
Injection Site Reactions				
Pain	29.4	0	33.9	0
Induration	6.4	0	8.2	0
Redness	6.0	0	12.9	0
Swelling	4.5	0	6.1	0
Systemic Reactions				
Headache**	32.5	0.9	39.5	1.0
Fatigue**	24.6	0.4	30.2	0.7
Malaise**	16.8	0.4	21.0	1.1
Arthralgia**	10.2	0.1	15.0	0.2
Diarrhea††	11.4	0.1	14.4	0.4
Anorexia‡‡	9.1	0.4	9.3	0.4
Chills§§	3.5	0.1	5.0	0.1
Fever***	2.8	0.1	0.5	0
Vomiting§§	1.6	0.3	1.4	0.3
Rash†††	1.5	-	1.2	-
Seizures†††	0	-	0	-

* Includes all subjects who provided data from comparative trials MTA02 and MTA04

† Includes all subjects who provided data from comparative trials MTA09 and MTA14

‡ Any denotes the proportion of participants reporting any reaction regardless of severity

§ Severe local reactions denotes swelling, redness or induration 2.0 inches in diameter or pain resulting in unwillingness to move the affected arm

** Severe: requiring bed rest

†† Severe: ≥ 5 episodes

‡‡ Severe: skipped ≥ 3 meals

§§ Severe: 3 episodes

*** Severe: ≥ 39.5°C

††† Severe: These solicited adverse events were reported as present or absent only

Data from Post-Marketing Experience

The following additional adverse events have been spontaneously reported during the post-marketing use of MENOMUNE® - A/C/Y/W-135. Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure. Decisions to include these events in labelling were based on one or more of the following factors: 1) severity of the event, 2) frequency of reporting, or 3) strength of causal connection to the vaccine.

Renal and Urinary Disorders

IgA nephropathy

Immune System Disorders

Allergic reactions, such as urticaria, pruritus, breathing difficulty, rash, and angioedema.

Nervous System Disorders

Vasovagal syncope, dizziness, and paraesthesia

Musculoskeletal and Connective Tissue Disorders

Myalgia

Physicians, nurses and pharmacists should report any adverse occurrences temporally related to the administration of the product in accordance with local requirements and to the Global Pharmacovigilance and Epidemiology Department, Sanofi Pasteur Limited, 1755 Steeles Avenue West, Toronto, ON, M2R 3T4, Canada. 1-888-621-1146 (phone) or 416-667-2435 (fax).

DRUG INTERACTIONS

Vaccine Drug Interactions

Immunosuppressive therapy or corticosteroid therapy may interfere with the development of the expected immune response. (See WARNINGS AND PRECAUTIONS).

Concomitant Vaccine Administration

MENOMUNE® - A/C/Y/W-135 should not be mixed in the same syringe with other parenterals (see DOSAGE AND ADMINISTRATION). Vaccines administered simultaneously, must be given using separate syringes at separate sites.

DOSAGE AND ADMINISTRATION

Recommended Dose

The immunizing dose is a single injection of 0.5 mL given subcutaneously.

For adults and children 2 years of age and older, primary immunization is a single 0.5 mL dose administered subcutaneously. For infants and children 3 - 23 months of age at risk of meningococcal Group A infection, primary immunization is two 0.5 mL doses 2 - 3 months apart.

For current information, consult the NACI updates on meningococcal vaccine recommendations.

For information on vaccine administration, see the current edition of the Canadian Immunization Guide or visit the Health Canada website.

Outbreak control

For control of outbreaks of serogroup C meningococcal disease in adolescents and adults, one dose of MENOMUNE® - A/C/Y/W-135 is recommended. (14)
For control of outbreaks of serogroup A meningococcal disease, MENOMUNE® - A/C/Y/W-135 is recommended as a single dose for adults and children ≥ 2 years of age. Children 3 to 23 months of age should receive two doses of vaccine given 3 months apart. For the control of outbreaks associated with serogroup Y or W-135 meningococci one dose of MENOMUNE® - A/C/Y/W-135 is recommended for persons ≥ 2 years of age. (14)

Pilgrims making the annual Hajj pilgrimage to Mecca should receive a single dose of MENOMUNE® - A/C/Y/W-135 at least 2 weeks before departure. (14)

For additional information on outbreak control please consult the Health Canada guidelines.

Administration

Inspect for extraneous particulate matter and/or discolouration before use. If these conditions exist, the product should not be administered.

The lyophilized vaccine should be a white or off-white to a light beige in colour. The diluent used for reconstitution should be clear.

Reconstitution of Freeze-Dried Product and Withdrawal from Stoppered Vial

Cleanse the stoppers of the vials containing the vaccine and the diluent with a suitable germicide before reconstitution. Do not remove the stoppers from either vial, or the metal seals holding them in place.

Withdraw the diluent into a syringe and inject slowly into the vial containing the vaccine. Swirl the vial gently. **Avoid foaming** since this will prevent withdrawal of the proper dose. Withdraw the required dose (0.5 mL) of the reconstituted vaccine into a syringe.

Aseptic technique must be used for withdrawal of each dose. Needles should not be recapped and should be disposed of properly. Use a separate sterile needle and syringe, or a sterile disposable unit for each individual recipient to prevent disease transmission. (See WARNINGS AND PRECAUTIONS)

MENOMUNE® - A/C/Y/W-135 when reconstituted should be a clear, colourless liquid.

Special care should be taken to avoid injecting the vaccine intradermally, intramuscularly, or intravenously since clinical studies have not been done to establish safety and efficacy of the vaccine using these routes of administration (See WARNINGS AND PRECAUTIONS).

MENOMUNE® - A/C/Y/W-135 should not be mixed in the same syringe with other parenterals. Vaccines administered simultaneously, must be given using separate syringes at separate sites (see DRUG INTERACTIONS).

Give the patient a permanent personal immunization record. In addition, it is essential that the physician or nurse record the immunization history in the permanent medical record of each patient. This permanent office record should contain the name of the vaccine, date given, dose, manufacturer and lot number.

OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of action

The presence of bactericidal anti-capsular meningococcal antibodies has been associated with protection from invasive meningococcal disease. (15) MENOMUNE® - A/C/Y/W-135 induces the production of bactericidal antibodies specific to the capsular polysaccharides of serogroups A, C, Y and W-135.

Serum bactericidal antibody (SBA) was established as a serological correlate of protection for group C meningococcal infection in studies in military recruits undertaken in the 1960s. These studies showed that those with naturally acquired SBA titres ≥1:4 measured using human complement (SBA-HC) were protected from meningitis caused by *Neisseria meningitidis* serogroup C. (15) An alternative complement source for the SBA is 3 to 4-week-old baby rabbit serum (SBA-BR). (16) While a group C SBA-BR titre ≥1:128 predicts protection against meningococcal serogroup C disease, it has been shown to underestimate vaccine efficacy; moreover, the cut off ≥1:8 was found to be the most consistent correlate with the observed efficacy of Meningococcal group C conjugate vaccine in the UK. (16) A serologic correlate that predicts clinical protection has not been established for serogroups A, Y and W-135.

Duration of Effect

Measurable levels of antibodies against the group A and C polysaccharides decrease markedly during the first 3 years following a single dose of vaccine. (17) This decrease in antibody occurs more rapidly in infants and young children than in adults.

STORAGE AND STABILITY

Store freeze-dried vaccine and reconstituted vaccine, when not in use, at 2° to 8°C (35° to 46°F). **Do not freeze**. The single dose vial should be used within 24 hours of reconstitution. Discard remainder of 10-dose vials of vaccine within 35 days after reconstitution. Discard product if exposed to freezing.

Do not use after expiration date.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Dosage Forms

The stopper of the vial for this product contains dry natural latex rubber.

Package of 1 x 1 dose vial of vaccine and 1 x 0.6 mL vial of diluent.

Package of 1 x 10 dose vial of vaccine and 1 x 6 mL vial of diluent.

Composition

Each single dose (0.5 mL) is formulated to contain:

Neisseria meningitidis group-specific polysaccharide antigens (A, C, Y and W-135)	50 µg each
thimerosal* (mercury derivative)	1:10,000
sodium chloride	4.25 - 4.75 mg
lactose (18)	2.5 - 5.0 mg
water for injection	q.s.

*for multidose presentation only

Vaccine Information Service: 1-888-621-1146 or 416-667-2779. Business hours: 8 a.m. to 5 p.m. Eastern Time, Monday to Friday.

Full product monograph available on request or visit us at www.sanofipasteur.ca

Product information as of July 2013.

Manufactured by:
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Swiftwater, PA, 18370 USA

Distributed by:
Sanofi Pasteur Limited
Toronto, Ontario, Canada

R10-0713 Canada
6496

PART II: SCIENTIFIC IMFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: Meningococcal Polysaccharide Vaccine, Groups A, C, Y and W-135 Combined.

Product Characteristics

MENOMUNE® - A/C/Y/W-135 is a freeze-dried preparation of the Group-specific polysaccharide antigens from *Neisseria meningitidis*, Group A, Group C, Group Y, and Group W-135 and is accompanied with diluent used for reconstitution. When reconstituted, the vaccine is a clear, colourless liquid.

Each 0.5 mL dose is formulated to contain 50 µg of "isolated product" from each of Groups A, C, Y and W-135 in an isotonic sodium chloride solution containing 2.5 mg to 5 mg of lactose that is added as a stabilizer. (18)

Group A, Group C, Group Y and Group W-135 *N. meningitidis* are cultivated on Mueller Hinton casein agar (19) and grown in Watson Scherp (20) casamino acid media. The purified polysaccharide is extracted from the *N. meningitidis* cells and separated from the media by procedures which include centrifugation, detergent precipitation, alcohol precipitation, solvent or organic extraction and diafiltration. No preservative is added during manufacture.

CLINICAL TRIALS

Clinical trials were conducted in healthy male and female subjects, 18 years of age and older where MENOMUNE® - A/C/Y/W-135 was administered to150 subjects and 25 subjects received placebo. In a clinical trial conducted in children, 73 subjects aged 2 to 12 years of age received MENOMUNE® - A/C/Y/W-135 .

MENOMUNE® - A/C/Y/W-135 was used as a control vaccine in five clinical trials (see Table 3) primarily designed to assess the safety and immunogenicity of Menactra® in children (2-10 years old), adolescents (11-18 years old) and adults (18-55 years old).

Study Demographics and Trial Design

Table 3: Summary of Study Design and Subject Demographics of Clinical Trials with MENOMUNE® - A/C/Y/W-135 as the Control Vaccine

Study #	Trial design (Safety and Immunogenicity)	Total subjects enrolled	Mean age (years) (Range)	Gender (Male/ Female)	Number of subjects receiving MENOMUNE® - A/C/Y/W-135
603-02	Comparison of Menactra® vs MENOMUNE® - A/C/Y/W-135	1398	3.6 (2-10)	731/667	702
MTA08*	Comparison of Menactra® vs MENOMUNE® - A/C/Y/W-135	3231	5.9 (2-10)	1632/ 1599	1519
MTA02	Comparison of Menactra® vs MENOMUNE® - A/C/Y/W-135	881	14.3 (11-17)	486/395	441
MTA09	Comparison of Menactra® vs MENOMUNE® - A/C/Y/W-135	2554	29.0 (18-55)	971/ 1583	1170
MTA04*	Comparison of Menactra® vs MENOMUNE® - A/C/Y/W-135	3242	15.5 (11-18)	1651/ 1591	972
MTA14	Lot Consistency and Comparison of Menactra® vs MENOMUNE® - A/C/Y/W-135	2040	34.5 (18-55)	722/ 1318	458

* Safety only

Study results

Immunogenicity

A study performed using 4 lots of MENOMUNE® - A/C/Y/W-135 in 150 adults showed at least a 4-fold increase in bactericidal antibodies to all groups in greater than 90 percent of the subjects. (21)

A study was conducted in 73 children 2 to 12 years of age. Post-immunization sera were not obtained on four children; seroconversion rates were calculated on 69 paired samples. Seroconversion rates as measured by bactericidal antibody were: Group A - 72%, Group C - 58%, Group Y - 90% and Group W-135 -82%. Seroconversion rates as measured by a 2-fold rise in antibody titres based on Solid Phase Radioimmunoassay were: Group A - 99%, Group C - 99%, Group Y - 97% and Group W-135 - 89%. (22)

In studies MTA02, MTA09 and 603-02, sera were obtained from participants before vaccination and approximately 28 days after vaccination. SBA-BR antibody titers for vaccine serogroups A, C, Y, and W-135 were measured. Immunogenicity was determined by the proportion of children 2-10 years of age achieving a pre-specified level of serum bactericidal antibody and the proportion of persons 11-55 years of age achieving a 4-fold increase from baseline in serum bactericidal antibody, for each serogroup.

The percentage of subjects, 2-10 years of age, (Study 603-02) who achieved seroprotection rates (SBA titre ≥1:8) observed at Day 28 post-vaccination were 98.3 %, 89.4%, 97.6% and 93.4% for serogroups A, C, Y and W-135, respectively (Table 4).

Table 4: Bactericidal Antibody Responses to MENOMUNE® - A/C/Y/W-135 28 Days After Vaccination in Children 2 to 10 Years of Age (10)

	Study 603-02 Menomune®-A/C/Y/W-135 N = 702				
Immune Response Criteria	**% Seroconversion (Day 0 titre <1:8 and Day 28 titre ≥1:32)**	**% ≥4-fold Rise**	**% with Day 28 titre ≥1:8**	**GMT on Day 28**	**GMT at 6 Months**
Serogroup A	94.7 (N = 265/280)	83.8	98.3	893	216
Serogroup C	80.1 (N = 293/366)	68.9	89.4	231	66
Serogroup Y	75.0 (N = 72/96)	45.6	97.6	408	240
Serogroup W-135	89.6 (N = 359/401)	85.4	93.4	426	137

The percentage of subjects, 11 – 18 years of age (Study MTA02), with a ≥4-fold rise in SBA-BR titer from baseline to Day 28 were 92.4%, 88.7%, 80.1% and 95.3% for serogroups A, C, Y, and W-135, respectively (Table 5). In subjects with an undetectable SBA-BR titer (< 8) at baseline, seroconversion rates (≥4-fold rise in Day 28 SBA-BR titers) following MENOMUNE® - A/C/Y/W-135 vaccination for serogroups A, C, Y, and W-135 ranged from 99% to 100%.

Table 5: Bactericidal Antibody Responses to MENOMUNE® - A/C/Y/W-135 Vaccine in Adolescents 11 to 18 Years of Age (23)

	Study MTA02 **Menomune®-A/C/Y/W-135** **N = 423**		
Immune Response Criteria	**% Seroconversion (Day 0 titre <1:8 and Day 28 ≥1:32)**	**% ≥4-fold Rise**	**GMT on Day 28**
Serogroup A	100 (N = 93/93)	92.4	3,246
Serogroup C	99.3 (N = 151/152)	88.7	1,639
Serogroup Y	100 (N = 47/47)	80.1	1,228
Serogroup W-135	99.3 (N = 138/139)	95.3	1,545

The percentage of participants, 18 -55 years of age (Study MTA09), with a ≥ 4-fold rise in SBA-BR titer from baseline to Day 28 were 84.6%, 89.7%, 79.4%, and 94.4% for serogroups A, C, Y, and W-135, respectively (Table 6). The percentage of seroconverters following MENOMUNE® - A/C/Y/W-135 vaccination, defined as participants with undetectable titers (< 8) on Day 0 achieving a ≥4-fold rise on Day 28 SBA-BR titers ranged from 96.9% to 99.3%.

Table 6: Bactericidal Antibody Responses to MENOMUNE® - A/C/Y/W-135 Vaccine in Adults 18 to 55 Years of Age (12)

	Study MTA09 Menomune®-A/C/Y/W-135 N = 1,098		
Immune Response Criteria	**% Seroconversion (Day 0 titre <1:8 and Day 28 titre ≥1:32)**	**% ≥4-fold Rise**	**GMT on Day 28**
Serogroup A	99.3 (N = 143/144)	84.6	4,114
Serogroup C	97.7 (N = 297/304)	89.7	3,469
Serogroup Y	96.9 (N = 221/228)	79.4	2,449
Serogroup W-135	99.1 (N = 325/328)	94.4	1,871

ADDITIONAL RELEVANT INFORMATION

N. meningitidis causes both endemic and epidemic disease, principally meningitis and meningococcemia.

The annual incidence of invasive meningococcal disease (IMD) in Canada has ranged between 0.5 and 2.1 per 100, 000 since the 1950s. Over the period 1995-2006, an average of 235 cases of IMD was reported annually. Using the 12-year average, the highest incidence is observed in infants less than 1 year of age (8.7 cases per 100 000), followed by children 1 through 4 years of age (2.3 per 100,000). The rates decrease in older children until adolescence and peak again in 15 through 19 year-olds (1.9 per 100,000) and 20 through 24 year-olds (1.0 per 100,000). Outbreaks of serogroup C were fairly common in the past. Between 1999 and 2001, 8 outbreaks of serogroup C meningococcal disease occurred in Canada. In more recent years, there has been a significant decline in incidence of serogroup C IMD. After serogroup C, serogroup B has caused the second highest burden of disease in Canada. Rates are particularly high in infants and children less than 4 years of age, but disease can occur at any age. Rates and numbers of serogroup Y IMD have remained stable over time. Although cases of serogroup Y IMD were reported in children and adolescents, most involved adults over the age of 25 years (median of 44 years of age during the period 1995 to 2006). IMD due to serogroups W-135 and A remains rare in Canada. (24) (25)

Globally, there are around 1.2 million cases of meningococcal disease annually. Although the disease occurs throughout the world, the most frequent and largest epidemics occur in the African meningitis belt, which includes all or part of 18 sub-Saharan countries. In this area, the majority of outbreaks are caused by *Neisseria meningitidis* serogroup A along with a smaller contribution by serogroup C. (26) More recently, countries in Africa outside of the "meningitis belt" have been affected by epidemic disease as a result of cross-border spread. (14) Since 2000, cases of serogroup W-135 invasive meningococcal disease have been reported in Saudi Arabia and subsequently in various other countries around the world. An epidemiologic association with international travel to Saudi Arabia or close contacts with pilgrims was established in most of these cases. (27) During 2002, a meningitis epidemic associated with W-135 was reported in Burkina Faso, and W-135 has now emerged as an epidemic strain in Africa. (27)

Certain immunodeficiencies result in a marked increase in the risk of meningococcal disease, these may include complement deficiencies (and properdin deficiency), hypogammaglobulinemia, anatomic and functional asplenia (e.g., sickle-cell disease). Individuals with human immunodeficiency virus may also be at increased risk for sporadic meningococcal disease. (14) Persons with cochlear implants have recently been identified as being at greater risk for meningitis. (28)

An elevated risk of meningococcal disease has been observed in the US among freshmen living in dormitories and university students in halls of residence in the UK. Clusters of cases of meningococcal disease in students have been reported in a number of countries and carriage rates increase rapidly amongst freshmen during the first week of the term in the UK. In this age group in Canada, as in other countries, there is an increase of the rate of meningococcal disease infection. (28) In US studies, as much as 83% of cases that occurred in this age group (15 - 24 years) were potentially vaccine preventable. (29) (30) Infection in this age group was associated with an unusually high case fatality ratio. (29)

Efficacy

The clinical efficacy of meningococcal vaccines containing polysaccharides of serogroup A and/or serogroup C has been well established from historical field trials and observational studies. (17) The serogroup A polysaccharide induces antibody in some children as young as 3 months of age, although a response comparable with that among adults is not achieved until 4 or 5 years of age; the serogroup C component is poorly immunogenic in recipients who are less than 18 to 24 months of age. (17) The serogroups A and C vaccines have demonstrated estimated clinical efficacies of 85% to 100% in older children and adults and are useful in controlling epidemics. Serogroups Y and W-135 polysaccharides are safe and immunogenic in adults and in children greater than 2 years of age. Although clinical protection has not been documented, vaccination with these polysaccharides induces bactericidal antibody. The antibody responses to each of the four polysaccharides in the quadrivalent vaccine are serogroup-specific and independent. (17)

Efficacy of serogroup A meningococcal vaccines was demonstrated in the 1970s in Africa and Finland, Egyptian school children aged 6 to 15 years showed 90% or greater protection during the first year after immunization with two different molecular sizes of serogroup A polysaccharide. (31) The higher molecular weight vaccine provided protection for at least three years. In Finland, a randomized controlled mass immunization trial with serogroup A vaccine was conducted in response to a serogroup A epidemic, in children three months to five years of age. Results

indicated 90 to 100% protection for three years. (31) In Rwanda, vaccination with bivalent A/C polysaccharide vaccine was performed in response to a serogroup A epidemic. A complete cessation of meningococcal disease was observed within two weeks of vaccination, yet the serogroup A carrier rate remained unchanged. (31)

Efficacy of serogroup C meningococcal vaccines was demonstrated in a field trial involving 20,000 troops in the US Army. Results suggested 90% efficacy under epidemic conditions which existed in basic training centers. (32) In Brazil, 67,300 young children aged 6 to 36 months, were vaccinated with serogroup C polysaccharide in response to a serogroup C epidemic. (31) Results indicated that the vaccine was not effective in children under 24 months of age and only 52% effective in children aged 24 to 36 months. (31) However, studies suggested that the vaccine used in this trial was less immunogenic than other lots of similar vaccine that were used in US children; also, it was shown that the molecular size of the vaccine was smaller than the serogroup C polysaccharide in the present vaccine. (32) Thus, it is quite probable that the current serogroup C polysaccharide vaccine is more effective. (31)

Studies evaluating the efficacy of meningococcal polysaccharide vaccines against disease caused by meningococcal serogroups Y and W-135 have not been conducted.

Duration of Effect

Measurable levels of antibodies against the group A and C polysaccharides decrease markedly during the first 3 years following a single dose of vaccine. (17) This decrease in antibody occurs more rapidly in infants and young children than in adults. Similarly, although vaccine-induced clinical protection probably persists in school children and adults for at least 3 years, the efficacy of the group A vaccine in young children may decrease markedly with the passage of time. In a 3-year study, efficacy declined from greater than 90% to less than 10% among children who were less than 4 years of age at the time of vaccination, whereas among children who were greater than or equal to 4 years of age when vaccinated, efficacy was 67% 3 years later. (17)

In New Zealand, a city-wide vaccine campaign in Auckland was conducted over 6 weeks among children 3 months to 13 years of age. Children 2 to 13 years of age received a single dose of monovalent Group A meningococcal vaccine. Children 3 to 23 months received two doses at least 1 month apart. However, only approximately 26% of the latter group received the recommended second dose. After 2.5 years of active surveillance (1987 to 1989) there were no cases of invasive Group A meningococcal disease in children appropriately vaccinated for age. (33)

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Vaccine Information Service: 1-888-621-1146 or 416-667-2779. Business hours: 8 a.m. to 5 p.m. Eastern Time, Monday to Friday.

Full product monograph available on request or visit us at www.sanofipasteur.ca

Product information as of July 2013.

Manufactured by:
Sanofi Pasteur Inc.
Swiftwater, PA, 18370 USA

Distributed by:
Sanofi Pasteur Limited
Toronto, Ontario, Canada

R10-0713 Canada
6496

IMPORTANT: PLEASE READ

PART III: CONSUMER INFORMATION

MENOMUNE® - A/C/Y/W-135

Meningococcal Polysaccharide Vaccine, Groups A, C, Y and W-135 Combined

This leaflet is part III of a three-part "Product Monograph" published when MENOMUNE® - A/C/Y/W-135 was approved for sale in Canada and is designed specifically for consumers. This leaflet is a summary and will not tell you everything about MENOMUNE® - A/C/Y/W-135. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

MENOMUNE® - A/C/Y/W-135 is a vaccine that is used to prevent meningococcal diseases and/or septicemia (blood poisoning) caused by bacteria called *Neisseria meningitidis* (serogroups A, C, Y and W-135). This vaccine may be given to persons 2 to 55 years old.

This vaccine does not prevent disease caused by other meningococcal bacteria other than serogroups A, C, Y and W-135.

Meningococcal diseases are very serious. Approximately 10% of people who get a meningococcal disease will die. Death may occur within 24-48 hours after symptoms appear. Of those who survive the disease, some (11 to 19%) will be permanently disabled. There are three kinds of meningococcal disease: meningococcemia, meningococcal meningitis and meningococcal pneumonia. Meningococcemia is the most serious form of the disease where up to 40% of those affected die.

What it does:

Menomune® - A/C/Y/W-135 vaccine causes your body to make substances called antibodies which help your body to fight disease caused by meningococcal serogroups A, C, Y and W-135. If a vaccinated person comes into contact with one of these germs, the body is usually ready to destroy it.

The amount of time it takes for your body to develop enough antibodies to protect you from meningococcal diseases can vary. It can take several days to a few weeks after your vaccination.

When it should not be used:

Do not give Menomune® - A/C/Y/W-135 to:

- persons who are known to have a severe allergy to any ingredient in the vaccine or its container, or who have had a severe allergic reaction after receiving a vaccine that contained similar ingredients.

What the medicinal ingredient is:

Each 0.5 mL dose of Menomune® - A/C/Y/W-135 contains: meningococcal A, C, Y and W-135 polysaccharides.

What the important nonmedicinal ingredients are:

The stopper for the single-dose vial and multi-dose vial contains dry natural rubber latex.

For a full listing of nonmedicinal ingredients see Part 1 of the product monograph.

What dosage forms it comes in:

Menomune® - A/C/Y/W-135 is supplied as a powder for solution which has to be reconstituted with the diluent. Once reconstituted, the clear colourless liquid vaccine is injected under the skin. A single dose is 0.5 mL.

WARNINGS AND PRECAUTIONS

If you or your child has any of the following conditions, talk to your doctor or nurse BEFORE you or your child receives Menomune® - A/C/Y/W-135:

- **A high fever or serious illness.** Delay the vaccination until the person is better.
- **An allergy to any component of the vaccine or the container.**
- **Pregnant or nursing women.** It is important that you understand the risks and benefits of vaccination. Menomune® - A/C/Y/W-135 should be given to a pregnant woman only if it is clearly needed. Tell the person giving you the injection if you are pregnant or breast-feeding.
- **A weakened immune system.** The vaccine may provide you with a lower level of protection than it does for people with healthy immune systems. If possible, try to postpone the vaccination until after you have completed the treatment that affects your immune system.
- **A bleeding disorder or taking blood-thinning medications.** Tell the person giving you the injection about your condition. The injection must be done carefully to prevent excessive bleeding.

If removal of the spleen (splenectomy) is planned, Menomune® - A/C/Y/W-135 should be given, if possible, 10 to 14 days before surgery.

INTERACTIONS WITH THIS MEDICATION

DO NOT mix Menomune® - A/C/Y/W-135 with other vaccines or medicinal products in the same syringe.

Menomune® - A/C/Y/W-135 may be given at the same time but at separate sites with:

- Yellow fever vaccine
- Typhoid Vaccine

PROPER USE OF THIS MEDICATION

Usual dose:

For persons 2 years of age and over, a single dose (0.5 mL) is recommended.

The vaccination should be given subcutaneously.

Overdose:

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed Dose:

Not applicable to this vaccine.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

A vaccine, like any medicine, may cause serious problems, such as severe allergic reactions. The risk of Menomune® - A/C/Y/W-135 causing serious harm is extremely small. The small risks associated with Menomune® - A/C/Y/W-135 are much less than the risks associated with getting the disease.

Tell your doctor, nurse or pharmacist as soon as possible if you do not feel well after having Menomune® - A/C/Y/W-135.

Serious side effects are extremely rare.

Some people who receive Menomune® - A/C/Y/W-135 may have mild side effects such as redness or pain at the site of injection, headache or fever. These side effects usually go away within a few days.

This is not a complete list of side effects. For any unexpected effects while taking Menomune® - A/C/Y/W-135 contact your doctor or pharmacist

HOW TO STORE IT

Store the vaccine in a refrigerator at 2° to 8°C (35° to 46°F). **Do not freeze.** Throw away the product if it has been exposed to freezing.

Do not use after the expiration date.

Keep out of reach of children.

REPORTING SUSPECTED SIDE EFFECTS

To monitor vaccine safety, the Public Health Agency of Canada collects case reports on adverse events following immunization.

For Health Care Professionals:
If a patient experiences an adverse event following immunization, please complete the appropriate Adverse Events following Immunization (AEFI) Form and send it to your local Health Unit in **your province/territory**.

For the General Public:
Should your child experience an adverse event following immunization, please ask your doctor, nurse, or pharmacist to complete the Adverse Events following Immunization (AEFI) Form.

If you have any questions or have difficulties contacting your local health unit, please contact Vaccine Safety Section at Public Health Agency of Canada:

By toll-free telephone: (1-866-844-0018)

By toll-free fax: (1-866-844-5931)

Email: caefi@phac-aspc.gc.ca

Web: http://www.phac-aspc.gc.ca/im/vs-sv/index-eng.php

Mail:
The Public Health Agency of Canada
Vaccine Safety Section
130 Colonnade Road
A/L 6502A
Ottawa, Ontario
K1A 0K9

NOTE: Should you require information related to the management of the side effect, please contact your health-care provider before notifying the Public Health Agency of Canada. The Public Health Agency of Canada does not provide medical advice

This document plus the full product monograph, prepared for health professionals can be found at: http://www.sanofipasteur.ca.

You may also contact the vaccine producer, Sanofi Pasteur Limited, for more information.
Telephone: 1-888-621-1146 (no charge) or 416-667-2779 (Toronto area).
Business hours: (8 a.m. to 5 p.m. EST Monday to Friday).

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