1. **NAME OF THE MEDICAL PRODUCT** : MENOMUNE® A/C/Y/W-135

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

2. **QUALITATIVE AND QUANTITATIVE COMPOSITION**

   Menomune – A/C/Y/W-135 vaccine consists of a sterile lyophilized preparation of the group-specific polysaccharide antigens from *N meningitidis*, Group A, Group C, Group Y and Group W-135. *N meningitidis* are cultivated with Mueller Hinton agar and Watson Scherp 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.

   Each 0.5 mL dose contains 50 mcg of polysaccharide from each of serogroups A, C, Y and W-135.

   For full list of excipients, see section 6.1

3. **PHARMACEUTICAL FORM**

   Menomune – A/C/Y/W-135 vaccine is supplied as a lyophilized vaccine, in a single dose or a multidose (10 dose) vial, with corresponding single dose or multidose vial of diluent. The lyophilized vaccine is reconstituted with the diluent. After reconstitution, each dose consists of a 0.5 mL suspension for injection.

4. **CLINICAL PARTICULARS**

   4.1 **Therapeutic indications**


   Menomune – A/C/Y/W-135 vaccine is not indicated for the prevention of meningitis caused by microorganisms other than *N. meningitidis* serogroups A, C, Y, and W-135. Menomune – A/C/Y/W-135 vaccine is not indicated for treatment of meningococcal infections.

   **Pediatric Use**

   Safety and effectiveness of Menomune – A/C/Y/W-135 vaccine in children below the age of 2 years have not been established.

   During a meningococcal serogroup A epidemic in sub-Saharan Africa, children 3 months to 16 years of age were vaccinated with a high molecular weight serogroup A/C meningococcal polysaccharide vaccine. In case-control studies, after 1 year of observation, vaccine efficacy against meningococcal serogroup A disease was estimated to be 87% [(90%
Confidence Interval (CI), 52% to 96%), overall. After 3 years, efficacy was estimated to be 67% (90% CI, 40% to 82%) among children who were 4-16 years of age at the time of vaccination and 8% (90% CI, -102% to 58%) among children who were 1-3 years of age at the time of vaccination.

The efficacy of a serogroup C meningococcal vaccine in infants and young children was evaluated in a placebo-controlled trial during a serogroup C epidemic in Brazil. Vaccine efficacy was estimated to be 12% (95% CI, -55% to 62%) among children 6 to 23 months of age and 55% (95% CI, -4% to 72%) among children 24 to 36 months of age.

**Geriatric Use**

Clinical studies of Menomune - A/C/Y/W-135 vaccine did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

### 4.2 Posology and method of administration

Primary immunization with Menomune – A/C/Y/W-135 vaccine consists of a single 0.5mL dose administered subcutaneously. The preferred site of administration is the deltoid region.

If Menomune – A/C/Y/W-135 vaccine is used for revaccination, the dose is 0.5mL administered subcutaneously.

The lyophilized vaccine should be a white or off-white color to a light beige color. The diluent used for reconstitution is a clear liquid.

Using a suitable size syringe, withdraw the supplied diluent (0.6 mL for single-dose presentation and 6.0 mL for multidose presentation) and inject into the vial containing the lyophilized vaccine. Swirl the vial until the vaccine is thoroughly dissolved. When reconstituted, the vaccine should be a clear, colorless liquid.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. If either of these conditions exist, the vaccine should not be administered.

Withdraw and administer a 0.5 mL dose of Menomune – A/C/Y/W-135 vaccine by subcutaneous injection.

Vaccine supplied in single dose vials should be used immediately after reconstitution. Vaccine supplied in multidose vials may be used for up to 35 days after reconstitution if stored at 2° to 8°C (35° to 46°F).

### 4.3 Contraindication

**Hypersensitivity**

Do not administer to anyone with a history of a severe allergic reaction (e.g., anaphylaxis) to Menomune – A/C/Y/W-135 vaccine or any component of the vaccine.
4.4 Special warnings and precautions for use

Latex

The stoppers to the vials of lyophilized vaccine and diluent contain dry natural latex rubber that may cause allergic reactions in latex sensitive persons.

Management of Acute Allergic Reactions

Appropriate medical treatment must be available to manage possible anaphylactic reactions following administration of the vaccine.

Moderate or Severe Acute Illness

To avoid diagnostic confusion between manifestations of an acute illness and possible vaccine adverse effects, vaccination with Menomune – A/C/Y/W-135 vaccine should be postponed in persons with moderate or severe acute illness.

Limitations of Vaccine Effectiveness

Menomune – A/C/Y/W-135 vaccine may not protect all recipients.

Altered Immunocompetence

Persons who are immunosuppressed, including persons receiving immunosuppressive therapy, may have a diminished immune response to Menomune – A/C/Y/W-135 vaccine.

4.5 Interaction with other medical products and forms of interaction

Do not mix Menomune – A/C/Y/W-135 vaccine with other vaccines in the same syringe or vial.

Immunosuppressive therapies may reduce the immune response to Menomune – A/C/Y/W-135 vaccine.

No safety and immunogenicity data are available on the concomitant administration of Menomune – A/C/Y/W-135 vaccine with other US licensed vaccines.

4.6 Pregnancy and lactation

Pregnancy

Pregnancy Category C. Animal reproduction studies have not been conducted with Menomune – A/C/Y/W-135 vaccine. It is also not known whether Menomune – A/C/Y/W-135 vaccine can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Menomune – A/C/Y/W-135 vaccine should be given to a pregnant woman only if clearly needed.
Lactation

It is not known whether Menomune – A/C/Y/W-135 vaccine is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Menomune – A/C/Y/W-135 vaccine is administered to a nursing woman.

4.7 Effects on the ability to drive and use machines

4.8 Undesirable effects

Data from Clinical Studies

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 clinical practice.

In three clinical trials primarily designed to assess the safety and immunogenicity of another vaccine, Menactra® [Meningococcal (Groups A, C, Y, W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine], participants were randomized to receive Menactra or Menomune – A/C/Y/W-135 vaccine, which was used as a control vaccine. In these three trials, 1519 children 2-10 years of age, 972 persons 11-18 years of age, and 1170 adults 18-55 years of age, respectively, received a dose of Menomune – A/C/Y/W-135 vaccine. Overall, of the children 2-10 years of age who received Menactra or Menomune – A/C/Y/W-135 vaccine, 68% were enrolled at US sites and 32% were enrolled at a Chilean site. The median ages of US and Chilean children were 6 and 5 years, respectively; 50.5% were males; and 92.0% were Caucasian. Among participants 11-55 years of age who received Menactra or Menomune – A/C/Y/W-135 vaccine, all were enrolled at US sites; 54.8% were female; 87.7% were Caucasian.

Solicited local and systemic reactions were monitored daily for 7 days post-vaccination using a diary card. Information on serious adverse events was collected at interim clinic visits and by telephone interview conducted 6 months post-vaccination. At least 94% of participants from the three studies completed the 6-month follow-up.

Serious Adverse Events

Across the three studies, serious adverse events within 6-months following Menomune – A/C/Y/W-135 vaccine were reported in 0.7% of 1519 children 2-10 years of age, 0.6% of 972 persons 11-18 years of age, and 1.7% of 1170 persons 18-55 years of age.

Solicited Adverse Events*

The most commonly reported solicited adverse events in US children 2-10 years of age were injection site pain, irritability and diarrhea. (Table 1)

The most commonly reported solicited adverse events in adolescents, ages 11 - 18 years, and adults, ages 18 - 55 years, were injection site pain, headache and fatigue. (Table 2)

* Events in Table 1 and Table 2 were collected in the clinical trials under “Solicited local and systemic reactions”.

4
<table>
<thead>
<tr>
<th>Event</th>
<th>Any</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>General Disorders and Administration Site Conditions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injection site reaction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain †</td>
<td>26.1</td>
<td>2.5</td>
<td>0.0</td>
</tr>
<tr>
<td>Redness‡</td>
<td>7.9</td>
<td>0.5</td>
<td>0.0</td>
</tr>
<tr>
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<td>4.2</td>
<td>0.6</td>
<td>0.0</td>
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<td>Swelling‡</td>
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<td>0.3</td>
<td>0.0</td>
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<tr>
<td>Systemic events</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever §</td>
<td>5.2</td>
<td>1.7</td>
<td>0.2</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anorexia</td>
<td></td>
<td></td>
<td>8.7</td>
</tr>
<tr>
<td>Vomiting ¶</td>
<td>2.7</td>
<td>0.7</td>
<td>0.6</td>
</tr>
<tr>
<td>Diarrhea #</td>
<td>11.8</td>
<td>2.5</td>
<td>0.3</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drowsiness **</td>
<td>11.2</td>
<td>2.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Irritability ††</td>
<td>12.2</td>
<td>2.6</td>
<td>0.6</td>
</tr>
<tr>
<td>Seizures ‡‡</td>
<td>0.0</td>
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<td>N/A</td>
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<tr>
<td>Musculoskeletal and connective tissue</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthralgia §§</td>
<td>5.3</td>
<td>0.7</td>
<td>0.0</td>
</tr>
<tr>
<td>Event</td>
<td>Any</td>
<td>Moderate</td>
<td>Severe</td>
</tr>
<tr>
<td>-------</td>
<td>-----</td>
<td>----------</td>
<td>--------</td>
</tr>
<tr>
<td>Skin and subcutaneous disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rash ‡‡</td>
<td>3.0</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

*N = The total number of participants with data. The N is for 1027 participants for all solicited events except fever (N=1019).

% is based on N.

† Moderate: Discomforting, interfered with or limited usual arm movement, Severe: Disabling, child unable to move arm.

‡ Moderate: 1.0–2.0 inches; Severe: ≥ 2.0 inches.

§ Oral equivalent temperature; Moderate: 38.4–39.4 ºC, Severe: ≥ 39.5 ºC.

|| Moderate: Skipped 2 meals, Severe: skipped ≥ 3 meals.

¶ Moderate: 2 episodes, Severe: ≥ 3 episodes.

# Moderate: 3-4 episodes, Severe: ≥ 5 episodes.

** Moderate: Interferes with normal activities, Severe: disabling, unwilling to engage in play or interaction with others.

†† Moderate: 1-3 hours duration, Severe: > 3 hours duration.

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

 §§ Moderate: Decreased range of motion due to pain or discomfort, Severe: unable to move major joints because of pain.

Table 2: Percentage of participants 11-55 years of age reporting solicited adverse events within 7 days following administration of Menomune - A/C/Y/W-135 vaccine

<table>
<thead>
<tr>
<th>Event</th>
<th>Study 1 N*=970</th>
<th>Study 2 N*=1159</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Participants 11-18 years of age</td>
<td>Participants 18-55 years of age</td>
</tr>
<tr>
<td>General Disorders and Administration Site Conditions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injection Site reaction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain†</td>
<td>28.7</td>
<td>48.1</td>
</tr>
<tr>
<td>Redness‡</td>
<td>5.7</td>
<td>16.0</td>
</tr>
<tr>
<td>Induration‡</td>
<td>5.2</td>
<td>11.0</td>
</tr>
<tr>
<td>Swelling‡</td>
<td>3.6</td>
<td>7.6</td>
</tr>
<tr>
<td>Event</td>
<td>Study 1 N*=970</td>
<td>Study 2 N*=1159</td>
</tr>
<tr>
<td>--------------------------------------------</td>
<td>----------------</td>
<td>----------------</td>
</tr>
<tr>
<td></td>
<td>Participants 11-18 years of age</td>
<td>Participants 18-55 years of age</td>
</tr>
<tr>
<td></td>
<td>Any Moderate Severe</td>
<td>Any Moderate Severe</td>
</tr>
<tr>
<td><strong>Systemic events</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue§</td>
<td>25.1 6.2 0.2</td>
<td>32.3 6.6 0.4</td>
</tr>
<tr>
<td>Malaise§</td>
<td>16.8 3.4 0.4</td>
<td>22.3 4.7 0.9</td>
</tr>
<tr>
<td>Chills§</td>
<td>3.5 0.4 0.1</td>
<td>5.6 1.0 0.0</td>
</tr>
<tr>
<td>Fever‖</td>
<td>3.0 0.3 0.1</td>
<td>0.5 0.1 0.0</td>
</tr>
<tr>
<td><strong>Gastrointestinal disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea¶</td>
<td>10.2 1.3 0.0</td>
<td>14.0 2.9 0.3</td>
</tr>
<tr>
<td>Anorexia#</td>
<td>7.7 1.1 0.2</td>
<td>9.9 1.6 0.4</td>
</tr>
<tr>
<td>Vomiting**</td>
<td>1.4 0.5 0.3</td>
<td>1.5 0.2 0.4</td>
</tr>
<tr>
<td><strong>Nervous system disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache††</td>
<td>29.3 6.5 0.4</td>
<td>41.8 8.9 0.9</td>
</tr>
<tr>
<td>Seizure‡‡</td>
<td>0.0 N/A N/A</td>
<td>0.0 N/A N/A</td>
</tr>
<tr>
<td><strong>Musculoskeletal and connective tissue disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthralgia§</td>
<td>10.2 2.1 0.1</td>
<td>16.0 2.6 0.1</td>
</tr>
<tr>
<td><strong>Skin and subcutaneous disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rash‡‡</td>
<td>1.4 N/A N/A</td>
<td>0.8 N/A N/A</td>
</tr>
</tbody>
</table>

*N=Total number of participants with data.
† Moderate: Discomforting, interfered with or limited usual arm movement, Severe: Disabling, unable to move arm.
‡ Moderate: 1.0–2.0 inches; Severe: > 2.0 inches.
§ Moderate: Interferes with normal activities, Severe: disabling, requires bed rest.
‖ Oral equivalent temperature. Study 1: Moderate: 38.5-39.4 ºC, Severe: ≥ 39.5ºC. Study 2: Moderate 39.0-39.9 ºC, Severe: ≥ 40.0 ºC.
¶ Moderate: 3-4 episodes, Severe: ≥ 5 episodes.
# Moderate: Skipped 2 meals, Severe: skipped ≥ 3 meals.
** Moderate: 2 episodes, Severe: ≥ 3 episodes.
†† Moderate: discomforting enough to interfere with activities, Severe: disabling requires bed rest and analgesics.
‡‡ These solicited adverse events were reported as present or absent only.
Data from Post-Marketing Experience

The following adverse events have been spontaneously reported during post-approval use of Menomune – A/C/Y/W-135 vaccine since 1993 through November 2008. 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 Menomune – A/C/Y/W-135 vaccine exposure.

The following adverse events were included based on severity, frequency of reporting or the strength of causal association to Menomune – A/C/Y/W-135 vaccine.

Immune system disorders
- Hypersensitivity, such as rash, urticaria, pruritus, dyspnoea, angioedema.

Nervous System Disorders
- Headache, vasovagal syncope, dizziness, paraesthesia, Guillain-Barré syndrome

Gastrointestinal disorders
- Nausea, vomiting, diarrhea

Musculoskeletal and Connective Tissue Disorders
- Myalgia, arthralgia

General Disorders and Administration Site Conditions
- Fever, injection site reaction, malaise, asthenia, chills, fatigue

4.9 Overdose

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

5.2 Pharmacokinetic properties

5.3 Preclinical safety data

Menomune – A/C/Y/W-135 vaccine has not been evaluated for carcinogenic or mutagenic potential or impairment of fertility.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Each dose of vaccine contains 2.5 mg to 5 mg of lactose added as a stabilizer.

The diluent (0.6 mL) for the single –dose presentation contains sterile, pyrogen-free distilled water without preservative. The diluent (6 mL) for the multi-dose presentation contains sterile,
pyrogen-free distilled water and thimerosal, a mercury derivative, which is added as a preservative for the reconstituted vaccine. Reconstituted vaccine from a multi-dose vial also contains 25 mcg mercury per dose.

6.2 Incompatibilities

6.3 Shelf life
   2 years

6.4 Special precautions for storage

   Store lyophilized vaccine, diluent, and reconstituted vaccine, when not in use, at 2° to 8°C (35° to 46°F). Do not freeze.

   Do not use after the expiration date shown on the vial labels of the lyophilized vaccine and diluent.

   Discard remainder of reconstituted vaccine from multidose vials within 35 days after reconstitution. Vaccine from single dose vials should be used immediately after reconstitution.

6.5 Nature and contents of container

   One single dose vial of lyophilized vaccine, with one 0.6 mL vial of diluent (contains no preservative).
   One 10 dose vial of lyophilized vaccine, with one 6.0 mL vial of diluent (contains preservative).

6.6 Special precautions for disposal and other handling

7. MARKETING AUTHORISATION HOLDER
   Sanofi Pasteur Ltd., Bangkok, Thailand

8. MARKETING AUTHORISATION NUMBER(S)
   1C 48/42

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
   15 March 1999

10. DATE OF REVISION OF THE TEXT
    January 2009
    Date of local approval: 10 March 2011

    (The above information is based on the currently approved leaflet)