

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Menactra® (Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine) safely and effectively. See full prescribing information for Menactra vaccine.

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

Initial U.S. Approval: 2005

-----RECENT MAJOR CHANGES-----

Indications and Usage (1) [4/2011]
Dosage and Administration (2) [4/2011]
Dosage Forms and Strengths (3) [12/2010]
Warnings and Precautions (5) [6/2011]

-----INDICATIONS AND USAGE-----

Menactra 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 does not prevent *N meningitidis* serogroup B disease. (1)

-----DOSAGE AND ADMINISTRATION-----

A 0.5 mL dose for intramuscular injection. (2)

- Children 9 through 23 months of age:
Two doses, three months apart.
- Individuals 2 through 55 years of age:
A single dose.

-----DOSAGE FORMS AND STRENGTHS-----

Liquid solution supplied in 0.5 mL single-dose vials (3)

-----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. (4)

-----WARNINGS AND PRECAUTIONS-----

- 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. (5.1)

-----ADVERSE REACTIONS-----

- Common (≥10%) solicited adverse events in infants and toddlers 9 and 12 months of age were injection site tenderness, erythema, and swelling; irritability, abnormal crying, drowsiness, appetite loss, vomiting, and fever. (6)
- Common (≥10%) solicited adverse events in individuals 2 through 55 years of age were injection site pain, redness, induration, and swelling; anorexia and diarrhea. Other common solicited adverse events were irritability and drowsiness (2-10 years of age), headache, fatigue, malaise, and arthralgia (11-55 years of age). (6)

To report SUSPECTED ADVERSE REACTIONS, contact Sanofi Pasteur Inc. at 1-800-822-2463 (1-800-VACCINE) or VAERS at 1-800-822-7967 or <http://vaers.hhs.gov>.

-----DRUG INTERACTIONS-----

- Pneumococcal antibody responses to some serotypes in Prevnar (PCV7) were decreased following co-administration of Menactra vaccine and PCV7. (7.1)

-----USE IN SPECIFIC POPULATIONS-----

- Safety and effectiveness of Menactra vaccine have not been established in children younger than 9 months of age, pregnant women, nursing mothers, and adults older than 55 years of age. (8.1, 8.3, 8.4, 8.5)
- A Pregnancy Registry is available. Contact Sanofi Pasteur Inc. at 1-800-822-2463. (8.1)

See 17 PATIENT_COUNSELING_INFORMATION.

Revised: November 2011

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1 **FULL PRESCRIBING INFORMATION:**

2 **1 INDICATIONS AND USAGE**

3 Menactra[®], Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid
4 Conjugate Vaccine, is indicated for active immunization to prevent invasive meningococcal
5 disease caused by *N meningitidis* serogroups A, C, Y and W-135. Menactra is approved for use in
6 individuals 9 months through 55 years of age. Menactra vaccine does not prevent *N meningitidis*
7 serogroup B disease.

8

9 **2 DOSAGE AND ADMINISTRATION**

10 **2.1 Preparation for Administration**

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

15

16 Withdraw the 0.5 mL dose of vaccine from the single-dose vial using a sterile needle and syringe.

17

18 **2.2 Dose and Schedule**

19 Menactra vaccine is administered as a 0.5 mL dose by intramuscular injection.

20 In children 9 through 23 months of age, Menactra is given as a 2-dose series three months apart.

21 Individuals 2 through 55 years of age receive a single dose.

22 Do not administer this product intravenously or subcutaneously.

23

1 **2.3 Revaccination**

2 The need for a booster dose of Menactra vaccine has not yet been determined.

3

4 **3 DOSAGE FORMS AND STRENGTHS**

5 Menactra vaccine is a liquid solution supplied in 0.5 mL single-dose vials. [See *Description (11)* for
6 a complete listing of ingredients.]

7

8 **4 CONTRAINDICATIONS**

9 Severe allergic reaction (eg, anaphylaxis) after a previous dose of a meningococcal capsular
10 polysaccharide-, diphtheria toxoid- or CRM₁₉₇-containing vaccine, or to any component of
11 Menactra vaccine [see *Description (11)*].

12

13 **5 WARNINGS AND PRECAUTIONS**

14 **5.1 Guillain-Barré Syndrome**

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

18

19 GBS has been reported in temporal relationship following administration of Menactra vaccine. (1)
20 (2) The risk of GBS following Menactra vaccination was evaluated in a post-marketing
21 retrospective cohort study [*Post-Marketing Experience (6.2)*].

22

23 **5.2 Preventing and Managing Allergic Vaccine Reactions**

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

6

7 **5.3 Altered Immunocompetence**

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

10

11 **5.4 Limitations of Vaccine Effectiveness**

12 Menactra vaccine may not protect all recipients.

13

14 **6 ADVERSE REACTIONS**

15 **6.1 Clinical Trials Experience**

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

19

20 *Children 9 Through 12 Months of Age*

21 The safety of Menactra vaccine was evaluated in four clinical studies that enrolled 3721
22 participants who received Menactra vaccine at 9 and 12 months of age. At 12 months of age these

1 children also received one or more other recommended vaccines [Measles, Mumps, Rubella and
2 Varicella Virus Vaccine Live (MMRV) or Measles, Mumps, and Rubella Virus Vaccine (MMR)
3 and Varicella Virus Vaccine Live (V) each manufactured by Merck & Co., Inc., Pneumococcal 7-
4 valent Conjugate Vaccine (Diphtheria CRM₁₉₇ Protein) manufactured by Wyeth Pharmaceuticals
5 Inc. (PCV7), Hepatitis A Vaccine manufactured by Merck & Co., Inc. (HepA). A control group of
6 997 children was enrolled at 12 months of age and received two or more childhood vaccines
7 [MMRV (or MMR + V), PCV7, HepA] at 12 months of age [see *Concomitant Vaccine*
8 *Administration* (14.3)]. Three percent of individuals received MMR and V, instead of MMRV, at
9 12 months of age.

10

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

17

18 ***Individuals 2 Through 55 Years of Age***

19 The safety of Menactra vaccine was evaluated in eight clinical studies that enrolled 10,057
20 participants aged 2-55 years who received Menactra vaccine and 5,266 participants who received
21 Menomune[®] – A/C/Y/W-135, Meningococcal Polysaccharide Vaccine, Groups A, C, Y and W-
22 135 Combined. There were no substantive differences in demographic characteristics between the
23 vaccine groups. Among Menactra vaccine recipients 2-55 years of age 24.0%, 16.2%, 40.4% and

1 19.4% were in the 2-10, 11-14, 15-25 and 26-55-year age groups, respectively. Among
2 Menomune – A/C/Y/W-135 vaccine recipients 2-55 years of age 42.3%, 9.3%, 30.0% and 18.5%
3 were in the 2-10, 11-14, 15-25 and 26-55-year age groups, respectively. The three primary safety
4 studies were randomized, active-controlled trials that enrolled participants 2-10 years of age
5 (Menactra vaccine, N=1713; Menomune – A/C/Y/W-135 vaccine, N=1519), 11-18 years of age
6 (Menactra vaccine, N=2270; Menomune – A/C/Y/W-135 vaccine, N=972) and 18-55 years of age
7 (Menactra vaccine, N=1384; Menomune – A/C/Y/W-135 vaccine, N=1170), respectively. Of the
8 3232 children 2-10 years of age, 68% of participants (Menactra vaccine, N=1164; Menomune –
9 A/C/Y/W-135 vaccine, N=1031) were enrolled at US sites and 32% (Menactra vaccine, N=549;
10 Menomune – A/C/Y/W-135 vaccine, N=488) of participants at a Chilean site. The median ages in
11 the Chilean and US subpopulations were 5 and 6 years, respectively. All adolescents and adults
12 were enrolled at US sites. As the route of administration differed for the two vaccines (Menactra
13 vaccine given intramuscularly, Menomune – A/C/Y/W-135 vaccine given subcutaneously), study
14 personnel collecting the safety data differed from personnel administering the vaccine.

15

16 ***Safety Evaluation***

17 Participants were monitored after each vaccination for 30 minutes for immediate reactions.
18 Solicited injection site and systemic reactions were recorded in a diary card for 7 consecutive days
19 after each vaccination. Participants were monitored for 28 days (30 days for infants and toddlers)
20 for unsolicited adverse events and for 6 months post-vaccination for visits to an emergency room,
21 unexpected visits to an office physician, and serious adverse events. Unsolicited adverse event
22 information was obtained either by telephone interview or at an interim clinic visit. Information

1 regarding adverse events that occurred in the 6-month post-vaccination time period was obtained
2 via a scripted telephone interview.

3

4 *Serious Adverse Events in All Safety Studies*

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

15

16 *Solicited Adverse Events in the Primary Safety Studies*

17 The most frequently reported solicited injection site and systemic adverse reactions within 7 days
18 following vaccination in children 9 months and 12 months of age ([Table 1](#)) were injection site
19 tenderness and irritability.

20

21 The most frequently reported solicited injection site and systemic adverse reactions in US children
22 aged 2 years through 10 years of age ([Table 2](#)) were injection site pain and irritability. Diarrhea,
23 drowsiness, and anorexia were also common.

1

2 The most commonly reported solicited injection site and systemic adverse reactions in
3 adolescents, ages 11-18 years ([Table 3](#)), and adults, ages 18-55 years ([Table 4](#)), were injection site
4 pain, headache and fatigue. Except for redness in adults, injection site reactions were more
5 frequently reported after Menactra vaccination than after Menomune – A/C/Y/W-135 vaccination.

6

- 1 **Table 1: Percentage of US Participants Reporting Solicited Adverse Reactions Within 7**
- 2 **Days Following Vaccine Administration at 9 Months and 12 Months of Age**

Reaction	Menactra vaccine at 9 months of age			Menactra + PCV7 ^a + MMRV ^b + HepA ^c vaccines at 12 months of age			PCV7 ^a + MMRV ^b + HepA ^c vaccines at 12 months of age		
	N ^d =998 - 1002			N ^d =898 - 908			N ^d =302 - 307		
	Any	Grade 2	Grade 3	Any	Grade 2	Grade 3	Any	Grade 2	Grade 3
Local/Injection Site									
Tenderness^e									
Menactra Site	37.4	4.3	0.6	48.5	7.5	1.3	-	-	-
PCV7 Site	-	-	-	45.6	9.4	1.6	45.7	8.3	0.3
MMRV Site	-	-	-	38.9	7.1	1.0	43.0	5.2	0.0
HepA Site	-	-	-	43.4	8.7	1.4	40.9	4.6	0.3
Erythema^f									
Menactra Site	30.2	2.5	0.3	30.1	1.3	0.1	-	-	-
PCV7 Site	-	-	-	29.4	2.6	0.2	32.6	3.0	0.7
MMRV Site	-	-	-	22.5	0.9	0.3	33.2	5.9	0.0
HepA Site	-	-	-	25.1	1.1	0.0	26.6	0.7	0.0
Swelling^f									
Menactra Site	16.8	0.9	0.2	16.2	0.9	0.1	-	-	-
PCV7 Site	-	-	-	19.5	1.3	0.4	16.6	1.3	0.7
MMRV Site	-	-	-	12.1	0.4	0.1	14.1	0.3	0.0
HepA Site	-	-	-	16.4	0.7	0.2	13.5	0.0	0.3
Systemic									
Irritability ^g	56.8	23.1	2.9	62.1	25.7	3.7	64.8	28.7	4.2
Abnormal crying ^h	33.3	8.3	2.0	40.0	11.5	2.4	39.4	10.1	0.7
Drowsiness ⁱ	30.2	3.5	0.7	39.8	5.3	1.1	39.1	5.2	0.7
Appetite loss ^j	30.2	7.1	1.2	35.7	7.6	2.6	31.9	6.5	0.7
Vomiting ^k	14.1	4.6	0.3	11.0	4.4	0.2	9.8	2.0	0.0
Fever ^l	12.2	4.5	1.1	24.5	11.9	2.2	21.8	7.3	2.6

- 3 ^a PCV7 (Prevnar[®]) = Pneumococcal 7-valent Conjugate Vaccine

- 1 ^bMMRV (ProQuad®) = Measles, Mumps, Rubella and Varicella Virus Vaccine Live
- 2 ^cHepA (VAQTA®) = Hepatitis A Vaccine, Inactivated
- 3 ^dN = The number of subjects with available data.
- 4 ^eGrade 2: cries and protests when injection site is touched, Grade 3: cries when injected limb is moved, or the
- 5 movement of the injected limb is reduced.
- 6 ^fGrade 2: ≥ 1.0 inches to < 2.0 inches, Grade 3: ≥ 2.0 inches.
- 7 ^gGrade 2: requires increased attention, Grade 3: inconsolable.
- 8 ^hGrade 2: 1 to 3 hours, Grade 3: > 3 hours.
- 9 ⁱGrade 2: not interested in surroundings or did not wake up for a feed/meal, Grade 3: sleeping most of the time or
- 10 difficult to wake up.
- 11 ^jGrade 2: missed 1 or 2 feeds/meals completely, Grade 3: refuses ≥ 3 feeds/meals or refuses most feeds/meals.
- 12 ^kGrade 2: 2 to 5 episodes per 24 hours, Grade 3: ≥ 6 episodes per 24 hours or requiring parenteral hydration.
- 13 ^lGrade 2: $> 38.5^{\circ}\text{C}$ to $\leq 39.5^{\circ}\text{C}$, Grade 3: $> 39.5^{\circ}\text{C}$.
- 14

1 **Table 2: Percentage of US Participants 2 Years Through 10 Years of Age Reporting**
2 **Solicited Adverse Reactions Within 7 Days Following Vaccine Administration**

Reaction	Menactra vaccine N ^a =1156 - 1157			Menomune – A/C/Y/W-135 vaccine N ^a =1027		
	Any	Grade 2	Grade 3	Any	Grade 2	Grade 3
Local/Injection Site						
Pain ^b	45.0	4.9	0.3	26.1	2.5	0.0
Redness ^c	21.8	4.6	3.9	7.9	0.5	0.0
Induration ^c	18.9	3.4	1.4	4.2	0.6	0.0
Swelling ^c	17.4	3.9	1.9	2.8	0.3	0.0
Systemic						
Irritability ^d	12.4	3.0	0.3	12.2	2.6	0.6
Diarrhea ^e	11.1	2.1	0.2	11.8	2.5	0.3
Drowsiness ^f	10.8	2.7	0.3	11.2	2.5	0.5
Anorexia ^g	8.2	1.7	0.4	8.7	1.3	0.8
Arthralgia ^h	6.8	0.5	0.2	5.3	0.7	0.0
Fever ⁱ	5.2	1.7	0.3	5.2	1.7	0.2
Rash ^j	3.4	-	-	3.0	-	-
Vomiting ^k	3.0	0.7	0.3	2.7	0.7	0.6
Seizure ^j	0.0	-	-	0.0	-	-

3 ^aN = The total number of subjects reporting at least one solicited reaction. The median age of participants was 6 years
4 in both vaccine groups.

5 ^bGrade 2: interferes with normal activities, Grade 3: disabling, unwilling to move arm.

6 ^cGrade 2: 1.0-2.0 inches, Grade 3: >2.0 inches.

7 ^dGrade 2: 1-3 hours duration, Grade 3: >3 hours duration.

8 ^eGrade 2: 3-4 episodes, Grade 3: ≥5 episodes.

9 ^fGrade 2: interferes with normal activities, Grade 3: disabling, unwilling to engage in play or interact with others.

- 1 ^g Grade 2: skipped 2 meals, Grade 3: skipped ≥ 3 meals.
- 2 ^h Grade 2: decreased range of motion due to pain or discomfort, Grade 3: unable to move major joints due to pain.
- 3 ⁱ Oral equivalent temperature; Grade 2: 38.4°C to 39.4°C, Grade 3: $\geq 39.5^\circ\text{C}$.
- 4 ^j These solicited adverse events were reported as present or absent only.
- 5 ^k Grade 2: 2 episodes, Grade 3: ≥ 3 episodes.
- 6 Note: During the study Grade 1, Grade 2, and Grade 3 were collected as Mild, Moderate, and Severe respectively.
- 7

1 **Table 3: Percentage of Participants 11 Years Through 18 Years of Age Reporting Solicited**
2 **Adverse Reactions Within 7 Days Following Vaccine Administration**

Reaction	Menactra vaccine N ^a =2264 - 2265			Menomune – A/C/Y/W-135 vaccine N ^a =970		
	Any	Grade 2	Grade 3	Any	Grade 2	Grade 3
Local/Injection Site						
Pain ^b	59.2 ^c	12.8 ^c	0.3	28.7	2.6	0.0
Induration ^d	15.7 ^c	2.5 ^c	0.3	5.2	0.5	0.0
Redness ^d	10.9 ^c	1.6 ^c	0.6 ^c	5.7	0.4	0.0
Swelling ^d	10.8 ^c	1.9 ^c	0.5 ^c	3.6	0.3	0.0
Systemic						
Headache ^e	35.6 ^c	9.6 ^c	1.1	29.3	6.5	0.4
Fatigue ^e	30.0 ^c	7.5	1.1 ^c	25.1	6.2	0.2
Malaise ^e	21.9 ^c	5.8 ^c	1.1	16.8	3.4	0.4
Arthralgia ^e	17.4 ^c	3.6 ^c	0.4	10.2	2.1	0.1
Diarrhea ^f	12.0	1.6	0.3	10.2	1.3	0.0
Anorexia ^g	10.7 ^c	2.0	0.3	7.7	1.1	0.2
Chills ^e	7.0 ^c	1.7 ^c	0.2	3.5	0.4	0.1
Fever ^h	5.1 ^c	0.6	0.0	3.0	0.3	0.1
Vomiting ⁱ	1.9	0.4	0.3	1.4	0.5	0.3
Rash ^j	1.6	-	-	1.4	-	-
Seizure ^j	0.0	-	-	0.0	-	-

3 ^aN = The number of subjects with available data.

4 ^bGrade 2: interferes with or limits usual arm movement, Grade 3: disabling, unable to move arm.

5 ^cDenotes $p < 0.05$ level of significance. The p values were calculated for each category and severity using Chi Square
6 test.

7 ^dGrade 2: 1.0-2.0 inches, Grade 3: >2.0 inches.

8 ^eGrade 2: interferes with normal activities, Grade 3: requiring bed rest.

1 ^fGrade 2: 3-4 episodes, Grade 3: ≥ 5 episodes.

2 ^gGrade 2: skipped 2 meals, Grade 3: skipped ≥ 3 meals.

3 ^hOral equivalent temperature; Grade 2: 38.5°C to 39.4°C, Grade 3: ≥ 39.5 °C.

4 ⁱGrade 2: 2 episodes, Grade 3: ≥ 3 episodes.

5 ^jThese solicited adverse events were reported as present or absent only.

6 Note: During the study Grade 1, Grade 2, and Grade 3 were collected as Mild, Moderate, and Severe respectively.

7

1 **Table 4: Percentage of Participants 18 Years Through 55 Years of Age Reporting Solicited**
2 **Adverse Reactions Within 7 Days Following Vaccine Administration**

Reaction	Menactra vaccine N ^a =1371			Menomune – A/C/Y/W-135 vaccine N ^a =1159		
	Any	Grade 2	Grade 3	Any	Grade 2	Grade 3
Local/Injection Site						
Pain ^b	53.9 ^c	11.3 ^c	0.2	48.1	3.3	0.1
Induration ^d	17.1 ^c	3.4 ^c	0.7 ^c	11.0	1.0	0.0
Redness ^d	14.4	2.9	1.1 ^c	16.0	1.9	0.1
Swelling ^d	12.6 ^c	2.3 ^c	0.9 ^c	7.6	0.7	0.0
Systemic						
Headache ^e	41.4	10.1	1.2	41.8	8.9	0.9
Fatigue ^e	34.7	8.3	0.9	32.3	6.6	0.4
Malaise ^e	23.6	6.6 ^c	1.1	22.3	4.7	0.9
Arthralgia ^e	19.8 ^c	4.7 ^c	0.3	16.0	2.6	0.1
Diarrhea ^f	16.0	2.6	0.4	14.0	2.9	0.3
Anorexia ^g	11.8	2.3	0.4	9.9	1.6	0.4
Chills ^e	9.7 ^c	2.1 ^c	0.6 ^c	5.6	1.0	0.0
Vomiting ^h	2.3	0.4	0.2	1.5	0.2	0.4
Fever ⁱ	1.5 ^c	0.3	0.0	0.5	0.1	0.0
Rash ^j	1.4	-	-	0.8	-	-
Seizure ^j	0.0	-	-	0.0	-	-

3 ^aN = The number of subjects with available data.

4 ^bGrade 2: interferes with or limits usual arm movement, Grade 3: disabling, unable to move arm.

5 ^cDenotes $p < 0.05$ level of significance. The p -values were calculated for each category and severity using Chi Square
6 test.

7 ^dGrade 2: 1.0-2.0 inches, Grade 3: >2.0 inches.

8 ^eGrade 2: interferes with normal activities, Grade 3: requiring bed rest.

9 ^fGrade 2: 3-4 episodes, Grade 3: ≥5 episodes.

1 ^g Grade 2: skipped 2 meals, Grade 3: skipped ≥ 3 meals.

2 ^h Grade 2: 2 episodes, Grade 3: ≥ 3 episodes.

3 ⁱ Oral equivalent temperature; Grade 2: 39.0°C to 39.9°C, Grade 3: $\geq 40.0^\circ\text{C}$.

4 ^j These solicited adverse events were reported as present or absent only.

5 Note: During the study Grade 1, Grade 2, and Grade 3 were collected as Mild, Moderate, and Severe respectively.

6

7 ***Adverse Events in Concomitant Vaccine Studies***

8 **Solicited Injection site and Systemic Reactions when Given with Routine Pediatric Vaccines**

9 For a description of the study design and number of participants [see *Clinical Studies,*
10 *Concomitant Vaccine Administration* (14.3)]. In the primary safety study, 1378 U.S. children were
11 enrolled to receive Menactra vaccine alone at 9 months of age and Menactra vaccine plus one or
12 more other routinely administered vaccines (MMRV, PCV7 and HepA) at 12 months of age
13 (N=961). Another group of children received two or more routinely administered vaccines
14 (MMRV, PCV7 and HepA vaccines) (control group, n=321) at 12 months of age. The frequency
15 of occurrence of solicited adverse events is presented in [Table 1](#). Participants who received
16 Menactra vaccine and the concomitant vaccines at 12 months of age described above reported
17 similar frequencies of tenderness, redness and swelling at the Menactra vaccine injection site and
18 at the concomitant vaccine injection sites. Tenderness was the most frequent injection site
19 reaction (48%, 39%, 46% and 43% at the Menactra vaccine, MMRV, PCV7 and HepA vaccine
20 sites, respectively). Irritability was the most frequent systemic reaction, reported in 62% of
21 recipients of Menactra vaccine plus concomitant vaccines, and 65% of control group. [See
22 *Concomitant Vaccine Administration* (14.3)].

23

1 **Solicited Injection site and Systemic Reactions when Given with Tetanus and Diphtheria**

2 **Toxoid Adsorbed Vaccine**

3 In a clinical study, rates of local and systemic reactions after Menactra vaccine and Tetanus and
4 Diphtheria Toxoid Adsorbed (Td) vaccine manufactured by Sanofi Pasteur Inc. were compared
5 [see *Drug Interactions* (7), and *Concomitant Vaccine Administration* (14.3) for study description].

6 Injection site pain was reported more frequently after Td vaccination than after Menactra

7 vaccination (71% versus 53%). The overall rate of systemic adverse events was higher when

8 Menactra and Td vaccines were given concomitantly than when Menactra vaccine was

9 administered 28 days after Td (59% versus 36%). In both groups, the most common reactions

10 were headache (Menactra vaccine + Td, 36%; Td + Placebo, 34%; Menactra vaccine alone, 22%)

11 and fatigue (Menactra vaccine + Td, 32%; Td + Placebo, 29%; Menactra vaccine alone, 17%).

12 Fever $\geq 40.0^{\circ}\text{C}$ occurred at $\leq 0.5\%$ in all groups.

13

14 **Solicited Injection site and Systemic Reactions when Given with Typhoid Vi Polysaccharide**

15 **Vaccine**

16 In a clinical study, rates of local and systemic reactions after Menactra vaccine and Typhoid Vi

17 Polysaccharide Vaccine, produced by Sanofi Pasteur SA were compared [see *Drug Interactions*

18 (7), *Concomitant Vaccine Administration* (14.3)] for a description of the concomitantly

19 administered vaccine, study design and number of participants. More participants experienced

20 pain after Typhoid vaccination than after Menactra vaccination (Typhoid + Placebo, 76% versus

21 Menactra vaccine + Typhoid, 47%). The majority (70%-77%) of injection site solicited reactions

22 for both groups at either injection site were reported as Grade 1 and resolved within 3 days post-

23 vaccination. In both groups, the most common systemic reaction was headache (Menactra vaccine

1 + Typhoid, 41%; Typhoid + Placebo, 42%; Menactra vaccine alone, 33%) and fatigue (Menactra
2 vaccine + Typhoid, 38%; Typhoid + Placebo, 35%; Menactra vaccine alone, 27%). Fever $\geq 40.0^{\circ}\text{C}$
3 and seizures were not reported in either group.

4

5 **6.2 Post-Marketing Experience**

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

12 • *Immune System Disorders*

13 Hypersensitivity reactions such as anaphylaxis/anaphylactic reaction, wheezing, difficulty
14 breathing, upper airway swelling, urticaria, erythema, pruritus, hypotension

15

16 • *Nervous System Disorders*

17 Guillain-Barré syndrome, paraesthesia, vasovagal syncope, dizziness, convulsion, facial
18 palsy, acute disseminated encephalomyelitis, transverse myelitis

19

20 • *Musculoskeletal and Connective Tissue Disorders*

21 Myalgia

22

23 ***Post-marketing Safety Study***

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

9

10 **7 DRUG INTERACTIONS**

11 **7.1 Concomitant Administration with Other Vaccines**

12 Menactra vaccine was concomitantly administered with Typhim Vi® [Typhoid Vi Polysaccharide
13 Vaccine] (Typhoid) and Tetanus and Diphtheria Toxoids Adsorbed, For Adult Use (Td), in
14 individuals 18 through 55 and 11 through 17 years of age, respectively. In children younger than 2
15 years of age, Menactra was co-administered with one or more of the following vaccines: PCV7,
16 MMR, V, MMRV, or HepA vaccine [see *Clinical Studies* (14) and *Adverse Reactions* (6)].

17

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

20

21 Pneumococcal antibody responses to some serotypes in PCV7 were decreased following co-
22 administration of Menactra vaccine and PCV7 [see *Concomitant Vaccine Administration* (14.3)].

23

1 Do not mix Menactra vaccine with other vaccines in the same syringe. When Menactra vaccine is
2 administered concomitantly with other injectable vaccines, the vaccines should be administered
3 with different syringes and given at separate injection sites.

4

5 **7.2 Immunosuppressive Therapies**

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

9

10 **8 USE IN SPECIFIC POPULATIONS**

11 **8.1 Pregnancy**

12 Pregnancy Category C

13 Animal reproduction studies have not been conducted with Menactra vaccine. It is also not known
14 whether Menactra vaccine can cause fetal harm when administered to a pregnant woman or can
15 affect reproduction capacity. There are no adequate and well controlled studies in pregnant
16 women. Menactra vaccine should only be given to a pregnant woman if clearly needed.

17 Assessment of the effects on animal reproduction has not been fully conducted with Menactra
18 vaccine as effects on male fertility in animals has not been evaluated. The effect of Menactra
19 vaccine on embryo-fetal and pre-weaning development was evaluated in one developmental
20 toxicity study in mice. Animals were administered Menactra vaccine on Day 14 prior to gestation
21 and during the period of organogenesis (gestation Day 6). The total dose given per time point was
22 0.1 mL/mouse via intramuscular injection (900 times the human dose, adjusted by body weight).

23 There were no adverse effects on pregnancy, parturition, lactation or pre-weaning development

1 noted in this study. Skeletal examinations revealed one fetus (1 of 234 examined) in the vaccine
2 group with a cleft palate. None were observed in the concurrent control group (0 of 174
3 examined). There are no data that suggest that this isolated finding is vaccine related, and there
4 were no vaccine related fetal malformations or other evidence of teratogenesis observed in this
5 study.

6

7 Healthcare providers are encouraged to register women who receive Menactra vaccine during
8 pregnancy in Sanofi Pasteur Inc.'s vaccination pregnancy registry by calling 1-800-822-2463.

9

10 **8.3 Nursing Mothers**

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

14

15 **8.4 Pediatric Use**

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

20

21 **8.5 Geriatric Use**

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

3

4 **11 DESCRIPTION**

5 Menactra[®], Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid
6 Conjugate Vaccine, is a sterile, intramuscularly administered vaccine that contains *Neisseria*
7 *meningitidis* serogroup A, C, Y and W-135 capsular polysaccharide antigens individually
8 conjugated to diphtheria toxoid protein. *N meningitidis* A, C, Y and W-135 strains are cultured on
9 Mueller Hinton agar (3) and grown in Watson Scherp (4) media. The polysaccharides are
10 extracted from the *N meningitidis* cells and purified by centrifugation, detergent precipitation,
11 alcohol precipitation, solvent extraction and diafiltration. To prepare the polysaccharides for
12 conjugation, they are depolymerized, derivatized, and purified by diafiltration. *Corynebacterium*
13 *diphtheriae* cultures are grown in a modified Mueller and Miller medium (5) and detoxified with
14 formaldehyde. The diphtheria toxoid protein is purified by ammonium sulfate fractionation and
15 diafiltration. The derivatized polysaccharides are covalently linked to diphtheria toxoid and
16 purified by serial diafiltration. The four meningococcal components, present as individual
17 serogroup-specific glycoconjugates, compose the final formulated vaccine. No preservative or
18 adjuvant is added during manufacture. Each 0.5 mL dose may contain residual amounts of
19 formaldehyde of less than 2.66 mcg (0.000532%), by calculation. Potency of Menactra vaccine is
20 determined by quantifying the amount of each polysaccharide antigen that is conjugated to
21 diphtheria toxoid protein and the amount of unconjugated polysaccharide present.

22

1 Menactra vaccine is manufactured as a sterile, clear to slightly turbid liquid. Each 0.5 mL dose of
2 vaccine is formulated in sodium phosphate buffered isotonic sodium chloride solution to contain 4
3 mcg each of meningococcal A, C, Y and W-135 polysaccharides conjugated to approximately 48
4 mcg of diphtheria toxoid protein carrier.

5

6 There is no latex in any component of the vial.

7

8 **12 CLINICAL PHARMACOLOGY**

9 **12.1 Mechanism of Action**

10 The presence of bactericidal anti-capsular meningococcal antibodies has been associated with
11 protection from invasive meningococcal disease. (6) (7) Menactra vaccine induces the production
12 of bactericidal antibodies specific to the capsular polysaccharides of serogroups A, C, Y and W-
13 135.

14

15 **13 NON-CLINICAL TOXICOLOGY**

16 **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

17 Menactra vaccine has not been evaluated for carcinogenic or mutagenic potential, or for
18 impairment of fertility.

19

20 **14 CLINICAL STUDIES**

21 **14.1 Efficacy**

22 The Serum Bactericidal Assay (SBA) used to test sera contained an exogenous complement
23 source that was either human (SBA-H) or baby rabbit (SBA-BR). (8)

1

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

11

12 **14.2 Immunogenicity**

13 *Children 9 through 12 Months of Age*

14 In a randomized, US, multi-center trial, children received Menactra vaccine at 9 months and 12
15 months of age. The first Menactra dose was administered alone, followed by a second Menactra
16 vaccine dose given alone (N=404), or with MMRV vaccine (N=302), or with PCV7 (N=422). For
17 all participants, sera were obtained approximately 30 days after last vaccination. There were no
18 substantive differences in demographic characteristics between the vaccine groups. The median
19 age range for administration of the first dose of Menactra was 278-279 days of age.

20

1 **Table 5: Bactericidal Antibody Responses^a 30 Days Following a Second Dose of Menactra**
 2 **Vaccine Administered Alone or Concomitantly Administered with MMRV or PCV7**
 3 **Vaccines at 12 Months of Age**

		Vaccinations administered at 12 months of age following a dose of Menactra at 9 months of age					
		Menactra vaccine		Menactra + MMRV vaccines		Menactra + PCV7 vaccines	
		(N=272-277) ^b		(N=177-180) ^b		(N=264-267) ^b	
Serogroup			(95% CI) ^c		(95% CI) ^c		(95% CI) ^c
A	% ≥1:8 ^d	95.6	(92.4; 97.7)	92.7	(87.8; 96.0)	90.5	(86.3; 93.8)
	GMT	54.9	(46.8; 64.5)	52.0	(41.8; 64.7)	41.0	(34.6; 48.5)
C	% ≥1:8 ^d	100.0	(98.7; 100.0)	98.9	(96.0; 99.9)	97.8	(95.2; 99.2)
	GMT	141.8	(123.5; 162.9)	161.9	(136.3; 192.3)	109.5	(94.1; 127.5)
Y	% ≥1:8 ^d	96.4	(93.4; 98.2)	96.6	(92.8; 98.8)	95.1	(91.8; 97.4)
	GMT	52.4	(45.4; 60.6)	60.2	(50.4; 71.7)	39.9	(34.4; 46.2)
W-135	% ≥1:8 ^d	86.4	(81.8; 90.3)	88.2	(82.5; 92.5)	81.2	(76.0; 85.7)
	GMT	24.3	(20.8; 28.3)	27.9	(22.7; 34.3)	17.9	(15.2; 21.0)

4 ^a Serum Bactericidal Assay with an exogenous human complement (SBA-H) source.

5 ^b N=Number of participants with at least one valid serology result from a blood sample obtained between Days 30 to
 6 44 post vaccination.

7 ^c 95% CIs for the proportions are calculated based on the Clopper-Pearson Exact method and normal approximation
 8 for that of the GMTs.

^d The proportion of participants achieving at least an SBA-H titer of 1:8 thirty days after the second dose of Menactra.

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 hSBA 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 hSBA 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* (6).]

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. In the study of children 2 through 10 years of age, the median age of participants was 3 years; 95% completed the study. In the adolescent trial, the median age for both groups was 14 years; 99% completed the study. In the adult trial, the median age for both groups was 24 years; 94% completed the study.

1 ***Immunogenicity in Children 2 through 10 Years of Age***

2 Of 1408 enrolled children 2 through 10 years of age, immune responses evaluated in a subset of
3 Menactra vaccine participants (2 through 3 years of age, n=52; 4-10 years of age, n=84) and
4 Menomune – A/C/Y/W-135 vaccine participants (2 through 3 years of age, n=53; 4-10 years of
5 age, n=84) were comparable for all four serogroups (Table 6).

6

7 **Table 6: Comparison of Bactericidal Antibody Responses^a to Menactra Vaccine and**
8 **Menomune – A/C/Y/W-135 Vaccine 28 Days after Vaccination for a Subset of Participants 2**
9 **through 3 Years of Age and 4 through 10 Years of Age**

		Ages 2 through 3 Years				Ages 4 through 10 Years			
		Menactra vaccine		Menomune – A/C/Y/W-135 vaccine		Menactra vaccine		Menomune – A/C/Y/W-135 vaccine	
		N ^b =48-52		N ^b =50-53		N ^b =84		N ^b =84	
Serogroup			(95% CI) ^c		(95% CI) ^c		(95% CI) ^c		(95% CI) ^c
A	% ≥1:8 ^d	73	(59,84)	64	(50,77)	81	(71,89)	55	(44,66)
	GMT	10	(8,13)	10	(7,12)	19	(14,26)	7	(6,9)
C	% ≥1:8 ^d	63	(48,76)	38	(25,53)	79	(68,87)	48	(37,59)
	GMT	27	(14,52)	11	(5,21)	28	(19,41)	12	(7,18)
Y	% ≥1:8 ^d	88	(75,95)	73	(59,84)	99	(94,100)	92	(84,97)
	GMT	51	(31,84)	18	(11,27)	99	(75,132)	46	(33,66)
W-135	% ≥1:8 ^d	63	(47,76)	33	(20,47)	85	(75,92)	79	(68,87)
	GMT	15	(9,25)	5	(3,6)	24	(18,33)	20	(14,27)

10 ^a Serum Bactericidal Assay with an exogenous human complement (SBA-H) source.

1 ^b N=Number of subset participants with at least one valid serology result at Day 0 and Day 28.

2 ^c The 95% CI for the Geometric Mean Titer (GMT) was calculated based on an approximation to the normal
3 distribution.

4 ^d The proportion of participants achieving at least an SBA-H titer of 1:8 was assessed using a 10% non-inferiority
5 margin and a one-sided Type 1 error rate of 0.025.

6

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

14

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

22

1 ***Immunogenicity in Adolescents 11 through 18 Years of Age***

2 Results from the comparative clinical trial conducted in 881 adolescents aged 11 through 18 years
3 showed that the immune responses to Menactra vaccine and Menomune – A/C/Y/W-135 vaccine
4 were similar for all four serogroups (Table 7).

5

6 In participants with undetectable pre-vaccination titers (ie, less than 1:8 at Day 0), seroconversion
7 rates (defined as a \geq 4-fold rise in Day 28 SBA-BR titers) were similar between the Menactra
8 vaccine and Menomune – A/C/Y/W-135 vaccine recipients. Menactra vaccine participants
9 achieved seroconversion rates of: 100%, Serogroup A (n=81/81); 99%, Serogroup C (n=153/155);
10 98%, Serogroup Y (n=60/61); 99%, Serogroup W-135 (n=161/164). The seroconversion rates for
11 Menomune – A/C/Y/W-135 vaccine recipients were: 100%, Serogroup A (n=93/93); 99%,
12 Serogroup C (n=151/152); 100%, Serogroup Y (n=47/47); 99%, Serogroup W-135 (n=138/139).

13

14 ***Immunogenicity in Adults 18 through 55 Years of Age***

15 Results from the comparative clinical trial conducted in 2554 adults aged 18 through 55 years
16 showed that the immune responses to Menactra vaccine and Menomune – A/C/Y/W-135 vaccine
17 were similar for all four serogroups (Table 7).

18

1 **Table 7: Comparison of Bactericidal Antibody Responses^a to Menactra Vaccine and**
 2 **Menomune – A/C/Y/W-135 Vaccine 28 Days after Vaccination for Participants 11 through**
 3 **18 Years of Age and 18 through 55 Years of Age**

		Ages 11 through 18 Years				Ages 18 through 55 Years			
		Menactra vaccine		Menomune – A/C/Y/W-135 vaccine		Menactra vaccine		Menomune – A/C/Y/W-135 vaccine	
		N ^b =423		N ^b =423		N ^b =1280		N ^b =1098	
Serogroup		(95% CI) ^c		(95% CI) ^c		(95% CI) ^c		(95% CI) ^c	
A	% ≥4-fold rise ^d	92.7	(89.8, 95.0)	92.4	(89.5, 94.8)	80.5	(78.2, 82.6)	84.6	(82.3, 86.7)
	GMT	5483	(4920, 6111)	3246	(2910, 3620)	3897	(3647, 4164)	4114	(3832, 4417)
C	% ≥4-fold rise ^d	91.7	(88.7, 94.2)	88.7	(85.2, 91.5)	88.5	(86.6, 90.2)	89.7	(87.8, 91.4)
	GMT	1924	(1662, 2228)	1639	(1406, 1911)	3231	(2955, 3533)	3469	(3148, 3823)
Y	% ≥4-fold rise ^d	81.8	(77.8, 85.4)	80.1	(76.0, 83.8)	73.5	(71.0, 75.9)	79.4	(76.9, 81.8)
	GMT	1322	(1162, 1505)	1228	(1088, 1386)	1750	(1597, 1918)	2449	(2237, 2680)
W-135	% ≥4-fold rise ^d	96.7	(94.5, 98.2)	95.3	(92.8, 97.1)	89.4	(87.6, 91.0)	94.4	(92.8, 95.6)
	GMT	1407	(1232, 1607)	1545	(1384, 1725)	1271	(1172, 1378)	1871	(1723, 2032)

4 ^a Serum Bactericidal Assay with baby rabbit complement (SBA-BR).

5 ^b N=Number of subset participants with at least one valid serology result at Day 0 and Day 28.

6 ^c The 95% CI for the Geometric Mean Titer (GMT) was calculated based on an approximation to the normal
 7 distribution.

8 ^d Menactra vaccine was non-inferior to Menomune – A/C/Y/W-135 vaccine. Non-inferiority was assessed by the
 9 proportion of participants with a 4-fold or greater rise in SBA-BR titer for *N meningitidis* serogroups A, C, Y and
 10 W-135 using a 10% non-inferiority margin and a one-sided Type I error rate of 0.05.

1

2 In participants with undetectable pre-vaccination titers (ie, less than 1:8 at Day 0), seroconversion
3 rates (defined as a ≥ 4 -fold rise in Day 28 SBA-BR titers) were similar between the Menactra
4 vaccine and Menomune – A/C/Y/W-135 vaccine recipients. Menactra vaccine participants
5 achieved seroconversion rates of: 100%, Serogroup A (n=156/156); 99%, Serogroup C
6 (n=343/345); 91%, Serogroup Y (n=253/279); 97%, Serogroup W-135 (n=360/373). The
7 seroconversion rates for Menomune – A/C/Y/W-135 vaccine recipients were: 99%, Serogroup A
8 (n=143/144); 98%, Serogroup C (n=297/304); 97%, Serogroup Y (n=221/228); 99%, Serogroup
9 W-135 (n=325/328).

10

11 **14.3 Concomitant Vaccine Administration**

12 ***MMRV (or MMR+V) or PCV7***

13 In a US, active-controlled trial, 1179 children received Menactra vaccine at 9 months and 12
14 months of age. At 12 months of age these children received Menactra concomitantly with MMRV
15 (N=616), or MMR + V (N=48), or PCV7 (N=250). Another group of 12-month old children
16 received MMRV + PCV7 (N=485). Sera were obtained approximately 30 days after the last
17 vaccinations. Measles, mumps, rubella and varicella antibody responses among children who
18 received Menactra vaccine and MMRV (or MMR and V) were comparable to corresponding
19 antibody responses among children who received MMRV and PCV7.

20

21 When Menactra was given concomitantly with PCV7, the non-inferiority criteria for comparisons
22 of pneumococcal IgG GMCs (upper limit of the two-sided 95% CI of the GMC ratio ≤ 2) were not

1 met for 3 of 7 serotypes (4, 6B, 18C). In a subset of subjects with available sera, pneumococcal
2 opsonophagocytic assay GMT data were consistent with IgG GMC data.

3

4 ***Td***

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

12

13 ***Typhim Vi***

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

1

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16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

- Vial, 1 Dose (5 vials per package). NDC 49281-589-05

16.2 Storage and Handling

Store at 2° to 8°C (35° to 46°F). DO NOT FREEZE. Frozen/previously frozen product should not be used. Do not use after the expiration date.

17 PATIENT COUNSELING INFORMATION

Vaccine Information Statements are required by the National Childhood Vaccine Injury Act of 1986 to be given prior to immunization to the patient, parent, or guardian. These materials are available free of charge at the Centers for Disease Control and Prevention (CDC) website (www.cdc.gov/vaccines.)

Inform the patients, parents or guardians about:

- Potential benefits and risks of immunization with Menactra vaccine.
- Potential for adverse reactions that have been temporally associated with administration of Menactra vaccine or other vaccines containing similar components.
- Reporting any adverse reactions to their healthcare provider.
- The Sanofi Pasteur Inc. pregnancy registry, as appropriate.

1 Menactra vaccine is a registered trademark of Sanofi Pasteur Inc.

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7 Manufactured by:

8 **Sanofi Pasteur Inc.**

9 Swiftwater PA 18370 USA

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