AUSTRALIAN PRODUCT INFORMATION

NAME OF THE MEDICINE

Menactra®

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

DESCRIPTION

Each 0.5 mL dose of vaccine contains:

Active ingredients:

- Meningococcal polysaccharide* Group A 4.0 mcg/dose
- Meningococcal polysaccharide* Group C 4.0 mcg/dose
- Meningococcal polysaccharide* Group Y 4.0 mcg/dose
- Meningococcal polysaccharide* Group W-135 4.0 mcg/dose
- Diphtheria toxoid protein Approximately 48 mcg/dose

* Each of the four polysaccharides is conjugated to diphtheria toxoid.

Excipients:

- Sodium chloride 4.35 mg

(within 0.85% Physiological Saline† and 0.5M Phosphate Buffered Saline§, pH 6.8)

- Sodium phosphate – dibasic anhydrous 0.348 mg

(within 0.5M Phosphate Buffered Saline§, pH 6.8)

- Sodium phosphate – monobasic 0.352 mg

(within 0.5M Phosphate Buffered Saline§, pH 6.8)

† 0.85% Physiological Saline is composed of sodium chloride in Water for Injections.

§ 0.5M Phosphate Buffered Saline is composed of sodium chloride, sodium phosphate dibasic anhydrous and sodium phosphate monobasic in Water for Injections.

Menactra vaccine is a sterile, clear to slightly turbid solution of *Neisseria meningitidis* purified capsular polysaccharides of groups A, C, Y and W-135, individually conjugated to a carrier protein. The protein is a purified *Corynebacterium diphtheriae* toxoid, *formalin-detoxified*. Each

0.5 mL dose of vaccine is formulated in sodium phosphate buffered isotonic sodium chloride solution. No preservative or adjuvant is added.

There is no latex in any component of the vial.

PHARMACOLOGY

Mechanism of action

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

CLINICAL TRIALS

Immunogenicity

Vaccine efficacy was inferred from the demonstration of immunologic equivalence to a meningococcal polysaccharide vaccine, Menomune®–A/C/Y/W-135, Meningococcal Polysaccharide Vaccine, Groups A, C, Y and W-135 Combined as assessed by Serum Bactericidal Assay (SBA). The SBA used to test sera contained an exogenous complement source that was either human (SBA-H) or, when correlated to SBA-H, baby rabbit (SBA-BR).

The response to vaccination in children 2–10 years old was evaluated by the proportion of subjects having an SBA-H antibody titre of 1:8 or greater, for each serogroup. In adolescents and adults, the response to vaccination was evaluated by the proportion of subjects with a 4-fold or greater increase in bactericidal antibody to each serogroup as measured by SBA-BR.

Immunogenicity was evaluated in three comparative, randomised, US, multi-centre, active controlled clinical trials that enrolled children (2–10 years old), adolescents (11–18 years old), and adults (18–55 years old). Participants received a 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.

In each of the trials, there were no substantive differences in demographic characteristics between the vaccine groups, between immunogenicity subsets or the overall study population.

Immunogenicity in Children

Of 1408 enrolled children 2–10 years old, immune responses evaluated in a subset of Menactra vaccine participants (2–3 years old, n=52; 4–10 years old, n=84) and Menomune–A/C/Y/W-135 vaccine participants (2–3 years old, n=53; 4–10 years old, n=84) were comparable for all four serogroups (**Table 1** and **Table 2**).

Table 1: Comparison of Bactericidal Antibody Responses* to Menactra vaccine and Menomune–A/C/Y/W-135 vaccine 28 Days After Vaccination for a Subset of Participants Aged 2–3 Years

		Menactra vaccine N‡=48-52		Menomune–A/C/Y/W-135 vaccine N‡=50-53	
Serogroup			(95% CI)§		(95% CI)§
A	% ≥ 1:8†	73	(59, 84)	64	(50, 77)
	GMT	10	(8, 13)	10	(7, 12)
C	% ≥ 1:8†	63	(48, 76)	38	(25, 53)
	GMT	27	(14, 52)	11	(5, 21)
Y	% ≥ 1:8†	88	(75, 95)	73	(59, 84)
	GMT	51	(31, 84)	18	(11, 27)
W-135	% ≥ 1:8†	63	(47, 76)	33	(20, 47)
	GMT	15	(9, 25)	5	(3, 6)

* Serum Bactericidal Assay with an exogenous human complement (SBA-H) source.

† The proportion of participants achieving at least an SBA-H titre of 1:8 was assessed using a 10% non-inferiority margin and a one-sided Type I error rate of 0.025.

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

§ The 95% CI for the Geometric Mean Titre (GMT) was calculated based on an approximation to the normal distribution.

Table 2: Comparison of Bactericidal Antibody Responses* to Menactra vaccine and Menomune–A/C/Y/W-135 vaccine 28 Days After Vaccination for a subset of Participants Aged 4–10 Years

		Menactra vaccine N‡=84		Menomune–A/C/Y/W-135 vaccine N‡=84	
Serogroup			(95% CI)§		(95% CI)§
A	% ≥ 1:8†	81	(71, 89)	55	(44, 66)
	GMT	19	(14, 26)	7	(6, 9)
C	% ≥ 1:8†	79	(68, 87)	48	(37, 59)
	GMT	28	(19, 41)	12	(7, 18)
Y	% ≥ 1:8†	99	(94, 100)	92	(84, 97)
	GMT	99	(75, 132)	46	(33, 66)
W-135	% ≥ 1:8†	85	(75, 92)	79	(68, 87)
	GMT	24	(18, 33)	20	(14, 27)

* Serum Bactericidal Assay with an exogenous human complement (SBA-H) source.

† The proportion of participants achieving at least an SBA-H titre of 1:8 was assessed using a 10% non-inferiority margin and a one-sided Type I error rate of 0.025.

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

§ The 95% CI for the Geometric Mean Titre (GMT) was calculated based on an approximation to the normal distribution.

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

In the subset of participants 4–10 years of age, percentages of participants that achieved seroconversion were similar between the Menactra vaccine and Menomune–A/C/Y/W-135 vaccine recipients. Menactra vaccine participants achieved seroconversion rates of: 69%, serogroup A (n=11/16); 81%, serogroup C (n=50/62); 98%, serogroup Y (n=45/46); 69%, serogroup W-135 (n=27/39). The seroconversion rates for Menomune–A/C/Y/W-135 vaccine recipients were 48%, serogroup A (n=10/21); 38%, serogroup C (n=19/50); 84%, serogroup Y (n=38/45); 68%, serogroup W-135 (n=26/38).

Immunogenicity in Adolescents

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

Table 3: Comparison of Bactericidal Antibody Responses* to Menactra Vaccine and Menomune–A/C/Y/W-135 Vaccine 28 Days after Vaccination for Participants Aged 11–18 Years

		Menactra vaccine N‡=423		Menomune–A/C/Y/W-135 vaccine N‡=423	
Serogroup			(95% CI)§		(95% CI)§
A	% ≥ 4-fold rise†	92.7	(89.8, 95.0)	92.4	(89.5, 94.8)
	GMT	5483	(4920, 6111)	3246	(2910, 3620)
C	% ≥ 4-fold rise†	91.7	(88.7, 94.2)	88.7	(85.2, 91.5)
	GMT	1924	(1662, 2228)	1639	(1406, 1911)
Y	% ≥ 4-fold rise†	81.8	(77.8, 85.4)	80.1	(76.0, 83.8)
	GMT	1322	(1162, 1505)	1228	(1088, 1386)
W-135	% ≥ 4-fold rise†	96.7	(94.5, 98.2)	95.3	(92.8, 97.1)
	GMT	1407	(1232, 1607)	1545	(1384, 1725)

* Serum Bactericidal Assay with baby rabbit complement (SBA-BR).

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

‡ N = Number of participants with valid serology results at Day 0 and Day 28.

§ The 95% CI for the Geometric Mean Titre (GMT) was calculated based on an approximation to the normal distribution.

In participants with undetectable pre-vaccination titres (i.e., less than 8 at Day 0), seroconversion rates (defined as a ≥ 4-fold rise in Day 28 SBA titres) were similar between the Menactra vaccine and Menomune–A/C/Y/W-135 vaccine recipients. Menactra vaccine participants achieved seroconversion rates of: 100%, serogroup A (n=81/81); 99%, serogroup C (n=153/155); 98%, serogroup Y (n=60/61); 99%, serogroup W-135 (n=161/164). The seroconversion rates for Menomune–A/C/Y/W-135 vaccine recipients were 100%, serogroup A (n=93/93); 99%, serogroup C (n=151/152); 100%, serogroup Y (n=47/47); 99%, serogroup W-135 (n=138/139).

Immunogenicity in Adults

Results from the comparative clinical trial conducted in 2554 adults aged 18–55 years showed that the immune responses to Menactra vaccine and Menomune–A/C/Y/W-135 vaccine were similar for all four serogroups (**Table 4**).

Table 4: Comparison of Bactericidal Antibody Responses* to Menactra Vaccine and Menomune–A/C/Y/W-135 Vaccine 28 Days After Vaccination for Participants Aged 18–55 Years

		Menactra vaccine N‡=1280		Menomune–A/C/Y/W-135 vaccine N‡=1098	
Serogroup			(95% CI)§		(95% CI)§
A	% ≥ 4-fold rise†	80.5	(78.2, 82.6)	84.6	(82.3, 86.7)
	GMT	3897	(3647, 4164)	4114	(3832, 4417)
C	% ≥ 4-fold rise†	88.5	(86.6, 90.2)	89.7	(87.8, 91.4)
	GMT	3231	(2955, 3533)	3469	(3148, 3823)
Y	% ≥ 4-fold rise†	73.5	(71.0, 75.9)	79.4	(76.9, 81.8)
	GMT	1750	(1597, 1918)	2449	(2237, 2680)
W-135	% ≥ 4-fold rise†	89.4	(87.6, 91.0)	94.4	(92.8, 95.6)
	GMT	1271	(1172, 1378)	1871	(1723, 2032)

* Serum Bactericidal Assay with baby rabbit complement (SBA-BR).

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

‡ N = Number of participants with valid serology results at Day 0 and Day 28.

§ The 95% CI for the GMT was calculated based on an approximation to the normal distribution.

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

Concomitant Vaccine Administration

Tetanus and Diphtheria

The concomitant use of Menactra vaccine and Tetanus and Diphtheria Toxoids Adsorbed, For Adult Use (Td, manufactured by Sanofi Pasteur Inc) was evaluated in a double-blind, randomised, controlled clinical trial conducted in 1021 participants aged 11–17 years. For meningococcal serogroups C, Y and W-135, the proportion of participants with a 4-fold or greater rise in SBA titre was higher when Menactra vaccine was given concomitantly with Td than when Menactra vaccine was given one month following Td. The clinical relevance of this finding has not been

fully evaluated. No interference was observed in the immune response to the tetanus and diphtheria components following concomitant vaccination.

Typhoid Vi Polysaccharide Vaccine, Typhim Vi®

The concomitant use of Menactra vaccine and Typhim Vi vaccine (recommended for certain travellers) was evaluated in a double-blind, randomised, controlled clinical trial conducted in 945 participants aged 18–55 years. The immune response to Menactra vaccine and to Typhim Vi vaccine when given concurrently was comparable to the immune response when Menactra vaccine or Typhim Vi vaccine was given alone.

INDICATIONS

Menactra vaccine is indicated for active immunisation of individuals 2 through 55 years of age for the prevention of invasive meningococcal disease caused by *N meningitidis* serogroups A, C, Y and W-135.

Menactra vaccine is not indicated for the prevention of meningitis caused by other microorganisms or for the prevention of invasive meningococcal disease caused by *N meningitidis* serogroup B.

Menactra vaccine is not indicated for treatment of meningococcal infections.

Menactra vaccine is not indicated for immunisation against diphtheria.

CONTRAINDICATIONS

Known hypersensitivity to any component of Menactra vaccine including diphtheria toxoid, or a life-threatening reaction after previous administration of a vaccine containing similar components, are contraindications to vaccine administration.

Known history of Guillain-Barré syndrome (see **PRECAUTIONS** section) is a contraindication to vaccine administration

Vaccination must be postponed in case of febrile or acute disease. However, a minor febrile or non-febrile illness, such as mild upper respiratory infection, is not usually a reason to postpone immunisation.

PRECAUTIONS

Do not administer by intravascular injection: ensure that the needle does not penetrate a blood vessel**.**

Prior to Vaccination

Anaphylaxis

As with all injectable vaccines, appropriate medical treatment and supervision should be readily available for immediate use in case of a rare anaphylactic reaction following the administration of vaccine. As a precautionary measure, adrenaline injection (1:1,000) must be immediately available in case of unexpected anaphylactic or serious allergic reactions.

Individual History

Before administration, all appropriate precautions should be taken to prevent adverse reactions. This includes a review of the patient's previous immunisation history, the presence of any contraindications to immunisation, the current health status, and history concerning possible sensitivity to the vaccine or similar vaccine.

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

Special Patient Groups

Thrombocytopenia or Bleeding Disorders

Menactra vaccine has not been evaluated in individuals with thrombocytopenia or bleeding disorders. As with any other vaccine administered intramuscularly, the vaccine risk versus benefit for individuals at risk of haemorrhage following intramuscular injection must be evaluated. If the decision is made to administer any product by intramuscular injection to such individuals, it should be given with caution, with steps taken to avoid the risk of haematoma formation following injection.

Immunosuppression

Menactra vaccine has been evaluated in about 300 Human Immunodeficiency Virus (HIV)-infected subjects. Menactra vaccine was safe and immunogenic in this population. The immune response to Menactra vaccine administered to other immunosuppressed individuals has not been studied. If the vaccine is used in individuals under immunosuppressive therapy, the expected immune response may not be obtained.

Guillain-Barré Syndrome

Guillain-Barré syndrome (GBS) has been reported in temporal relationship following administration of Menactra vaccine. An early evaluation of post-marketing adverse events suggested a potential for an increased risk of GBS following Menactra vaccination. However, a recent multi-site retrospective cohort and nested case control study involving over 12 million adolescents, of whom 1.4 million received Menactra vaccine, found no evidence of increased GBS risk associated with the use of Menactra vaccine. Nonetheless, individuals previously

diagnosed with GBS should not receive Menactra vaccine (see **ADVERSE EFFECTS** and **CONTRAINDICATIONS**).

Protection

Menactra vaccine may not protect 100% of individuals.

Menactra vaccine will only protect against *N meningitidis* A, C, Y and W-135 serogroups and will not protect against any other microorganisms.

Although an antibody response to diphtheria toxoid may occur, Menactra vaccine should not be considered as an immunising agent against diphtheria. No changes in the schedule for administering routine vaccines containing diphtheria toxoid are recommended.

Effects on fertility

There were no effects on the mating performance or fertility of female mice intramuscularly injected with Menactra vaccine (at one fifth of the clinical dose) two weeks prior to mating. The effect of Menactra vaccine on male fertility has not been evaluated (see also Use in Pregnancy).

Use in Pregnancy (Category B2)

In female mice intramuscularly injected with Menactra vaccine (at one fifth of the clinical dose) two weeks prior to mating and on gestation days 6 and 18, there were no significant toxicological effects in the dams, their foetuses or pups. Adequate human data on the use of Menactra vaccine during pregnancy are not available. The vaccine should be used during pregnancy only when clearly needed, such as during an outbreak or prior to necessary travel to an endemic area, and only following an assessment of the risks and benefits.

Sanofi Pasteur maintains a pregnancy registry to monitor foetal outcomes of pregnant women exposed to Menactra vaccine. Healthcare providers are encouraged to inform sanofi pasteur of any pregnant women who receive Menactra vaccine for their inclusion in the vaccination pregnancy registry by calling 1800 829 468 (in Australia) or 0800 727 838 (in New Zealand).

Use in Lactation

It is not known whether the active substances included in the vaccine are excreted in human milk, but antibodies to the polysaccharides have been found to be transferred to the suckling offspring of mice.
Animal studies conducted in mice have not shown any harmful effect on the postnatal development of offspring exposed through breastfeeding to Menactra-induced maternal antibodies. However, the effect on breast-fed infants of the administration of Menactra to their mothers has not been studied. The potential benefits to the mother and risks to the infant should be considered before administering Menactra vaccine to a nursing woman.

Paediatric Use

Menactra vaccine is approved for use in children from 2 years of age.

Use in the Elderly

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

Genotoxicity

No genotoxicity studies have been conducted with Menactra vaccine.

Carcinogenicity

No carcinogenicity studies have been conducted with Menactra vaccine.

Effect on Laboratory Tests

Interference of Menactra with laboratory tests has not been studied.

INTERACTIONS WITH OTHER MEDICINES

For information regarding concomitant administration of Menactra vaccine with other vaccines, see **CLINICAL TRIALS** and **ADVERSE EFFECTS** sections.

If the vaccine is used in individuals under immunosuppressive therapy, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs, and corticosteroids (used in greater than physiologic doses), the expected immune response may not be obtained.

Menactra must not be mixed with any vaccine in the same syringe. Separate injection sites should be used in case of concomitant administration.

ADVERSE EFFECTS

Clinical Trials Experience

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

The safety of Menactra vaccine was evaluated in 8 clinical studies that enrolled 10,057 participants aged 2–55 years who received Menactra vaccine and 5266 participants who received Menomune–A/C/Y/W-135 vaccine. The three primary safety studies were randomised, active-controlled trials that enrolled participants 2–10, 11–18 and 18–55 years of age, respectively.

Serious Adverse Events in All Safety Studies

Serious adverse events reported within a 6-month time period following vaccination in children 2–10 years old occurred at a rate of 0.6% following Menactra vaccine and at a rate of 0.7% following Menomune–A/C/Y/W-135 vaccine. Serious adverse events reported within a 6-month time period following vaccination in adolescents and adults occurred at a rate of 1.0% following Menactra vaccine and at a rate of 1.3% following Menomune–A/C/Y/W-135 vaccine.

Solicited Adverse Events in the Primary Safety Studies

The most frequently reported solicited local and systemic adverse reactions in children aged 2–10 years (**Table 5**) were injection site pain and irritability, respectively. Injection site redness, induration or swelling, diarrhoea, and drowsiness were also very common. . In adolescents, ages 11-18 years (**Table 6**), and adults, ages 18-55 years (**Table 7**), the most commonly reported were injection site pain, headache and fatigue. Except for redness in adults, local reactions were more frequently reported after Menactra vaccination than after Menomune–A/C/Y/W-135 vaccination.

Table 5: Percentage of US Participants 2–10 Years of Age Reporting Solicited Adverse Reactions Within 7 Days Following Vaccine Administration

	Menactra vaccine *N=1157			**Menomune–A/C/Y/W-135 vaccine *N=1027**		
Reaction	**Any**	**Moderate**	**Severe**	**Any**	**Moderate**	**Severe**
Redness†	21.8	4.6	3.9	7.9	0.5	0.0
Swelling†	17.4	3.9	1.9	2.8	0.3	0.0
Induration†	18.9	3.4	1.4	4.2	0.6	0.0
Pain‡	45.0	4.9	0.3	26.1	2.5	0.0
Drowsiness§	10.8	2.7	0.3	11.2	2.5	0.5
Irritability‖	12.4	3.0	0.3	12.2	2.6	0.6
Arthralgia¶	6.8	0.5	0.2	5.3	0.7	0.0
Diarrhoea#	11.1	2.1	0.2	11.8	2.5	0.3
Anorexia**	8.2	1.7	0.4	8.7	1.3	0.8
Fever††	5.2	1.7	0.3	5.2	1.7	0.2
Vomiting‡‡	3.0	0.7	0.3	2.7	0.7	0.6
Rash§§	3.4			3.0		
Seizure§§	0.0			0.0		

* N = The total number of subjects reporting at least one solicited reaction. The median age of participants was 6 years in both vaccine groups.

† Moderate: 1.0-2.0 inches, Severe: >2.0 inches.

‡ Moderate: interferes with normal activities, Severe: disabling, unwilling to move arm.

§ Moderate: interferes with normal activities, Severe: disabling, unwilling to engage in play or interact with others.

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

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

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

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

†† Oral equivalent temperature; Moderate: 38.4-39.4ºC, Severe: ≥ 39.5ºC.

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

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

Table 6: Percentage of Participants 11–18 Years of Age Reporting Solicited Adverse Reactions Within 7 Days Following Vaccine Administration

	Menactra vaccine N*=2264			**Menomune–A/C/Y/W-135 vaccine N*=970**		
Reaction	**Any**	**Moderate**	**Severe**	**Any**	**Moderate**	**Severe**
Redness‡	10.9†	1.6†	0.6†	5.7	0.4	0.0
Swelling‡	10.8†	1.9†	0.5†	3.6	0.3	0.0
Induration‡	15.7†	2.5†	0.3	5.2	0.5	0.0
Pain§	59.2†	12.8†	0.3	28.7	2.6	0.0
Headache‖	35.6†	9.6†	1.1	29.3	6.5	0.4
Fatigue‖	30.0†	7.5	1.1†	25.1	6.2	0.2
Malaise‖	21.9†	5.8†	1.1	16.8	3.4	0.4
Arthralgia‖	17.4†	3.6†	0.4	10.2	2.1	0.1
Diarrhoea¶	12.0	1.6	0.3	10.2	1.3	0.0
Anorexia#	10.7†	2.0	0.3	7.7	1.1	0.2
Chills‖	7.0†	1.7†	0.2	3.5	0.4	0.1
Fever**	5.1†	0.6	0.0	3.0	0.3	0.1
Vomiting††	1.9	0.4	0.3	1.4	0.5	0.3
Rash‡‡	1.6			1.4		
Seizure‡‡	0.0			0.0		

* N = The number of subjects with available data.

† Denotes $\rho < 0.05$ level of significance. The *p* values were calculated for each category and severity using Chi Square test.

‡ Moderate: 1.0-2.0 inches, Severe: >2.0 inches.

§ Moderate: Interferes with or limits usual arm movement, Severe: Disabling, unable to move arm.

‖ Moderate: Interferes with normal activities, Severe: Requiring bed rest.

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

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

** Oral equivalent temperature; Moderate: 38.5-39.4ºC, Severe: ≥ 39.5ºC.

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

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

Table 7: Percentage of Participants 18–55 Years of Age Reporting Solicited Adverse Reactions Within 7 Days Following Vaccine Administration

	Menactra vaccine N*=1371			**Menomune–A/C/Y/W-135 vaccine N*=1159**		
Reaction	**Any**	**Moderate**	**Severe**	**Any**	**Moderate**	**Severe**
Redness‡	14.4	2.9	1.1†	16.0	1.9	0.1
Swelling‡	12.6†	2.3†	0.9†	7.6	0.7	0.0
Induration‡	17.1†	3.4†	0.7†	11.0	1.0	0.0
Pain§	53.9†	11.3†	0.2	48.1	3.3	0.1
Headache‖	41.4	10.1	1.2	41.8	8.9	0.9
Fatigue‖	34.7	8.3	0.9	32.3	6.6	0.4
Malaise‖	23.6	6.6†	1.1	22.3	4.7	0.9
Arthralgia‖	19.8†	4.7†	0.3	16.0	2.6	0.1
Diarrhoea¶	16.0	2.6	0.4	14.0	2.9	0.3
Anorexia#	11.8	2.3	0.4	9.9	1.6	0.4
Chills‖	9.7†	2.1†	0.6†	5.6	1.0	0.0
Fever**	1.5†	0.3	0.0	0.5	0.1	0.0
Vomiting††	2.3	0.4	0.2	1.5	0.2	0.4
Rash‡‡	1.4			0.8		
Seizure‡‡	0.0			0.0		

* N = The number of subjects with available data.

† Denotes $\rho < 0.05$ level of significance. The *p* values were calculated for each category and severity using Chi Square test.

‡ Moderate: 1.0-2.0 inches, Severe: >2.0 inches.

§ Moderate: Interferes with or limits usual arm movement, Severe: Disabling, unable to move arm.

‖ Moderate: Interferes with normal activities, Severe: Requiring bed rest.

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

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

** Oral equivalent temperature; Moderate: 39.0-39.9ºC, Severe: ≥40.0ºC.

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

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

Adverse Events in Concomitant Vaccine Studies

Local and Systemic Reactions when Given with Td Vaccine

The two vaccine groups reported similar frequencies of pain, induration, redness and swelling at the Menactra injection site, as well as, at the Td injection site. Pain was the most frequent local reaction reported at both the Menactra and Td injection sites.

The overall rate of systemic adverse events was higher when Menactra and Td vaccines were given concomitantly than when Menactra vaccine was administered 28 days after Td. In both groups, the most common reactions were headache and fatigue.

Local and Systemic Reactions when Given with Typhim Vi Vaccine

The two vaccine groups reported similar frequencies of pain, induration, redness and swelling at the Menactra injection site, as well as, at the Typhim Vi injection site. Pain was the most frequent local reaction reported at both the Menactra and Typhim Vi injection sites. More participants experienced pain after Typhim Vi vaccination than after Menactra vaccination (76% versus 47%). The majority (70%-77%) of local solicited reactions for both groups at either injection site were reported as mild and resolved within 3 days post-vaccination. In both groups, the most common systemic reaction was headache and fatigue.

Post-Marketing Reports

Based on spontaneous reporting, the following additional adverse events have been reported during the commercial use of Menactra vaccine. These events have been very rarely reported. However, because these events were reported voluntarily from a population of uncertain size, it is not always possible to reliably calculate their frequency or to establish a causal relationship to Menactra vaccine exposure.

Immune system disorders:

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

Nervous system disorders:

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

Musculoskeletal and connective tissue disorders:

Myalgia

DOSAGE AND ADMINISTRATION

Menactra vaccine should be administered as a single 0.5 mL injection by the **intramuscular** route, preferably in the deltoid region.

Do not administer by intravascular injection.

Avoid injecting the vaccine intradermally or subcutaneously since clinical studies have not been conducted to establish safety and efficacy of the vaccine using these routes of administration.

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

There are limited data available on the length of time that should lapse before administration of Menactra vaccine in those individuals who have been previously vaccinated with other meningococcal vaccine.

For further information, refer to the current National Immunisation Handbook.

Parenteral drug products should be inspected visually for container integrity, particulate matter and discoloration prior to administration, whenever solution and container permit.

Menactra vaccine must not be mixed with any vaccine in the same syringe. Therefore, separate injection sites and different syringes should be used in case of concomitant administration.

Product is for single use in one patient only. Discard any residue.

OVERDOSE

No case of overdose has been reported.

PRESENTATION AND STORAGE CONDITIONS

Presentation

Vial, 1 Dose

Packs of 1 vial (marketed) or 5 vials (not marketed)

Storage

Store at 2°C to 8°C (Refrigerate. Do not freeze). Product that has been exposed to freezing should not be used. Do not use after expiration date.

Protect from light.

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POISON SCHEDULE OF THE MEDICINE

S4 Prescription Only Medicine

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (ARTG)

26 July 2011

DATE OF MOST RECENT AMENDMENT

20 June 2014

Menactra is a registered trademark of sanofi pasteur and its subsidiaries.