NEW ZEALAND DATA SHEET

1 MENACTRA (SOLUTION FOR INJECTION)

Menactra® 0.5 mL solution for injection.

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

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

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.

Menactra 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.

For the full list of excipients, see Section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Menactra is indicated for active immunisation in individuals from 9 months through 55 years of age for the prevention of invasive meningococcal disease caused by *N meningitidis* serogroups A, C, Y and W-135.

Menactra 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 is not indicated for treatment of meningococcal infections.

Menactra is not indicated for immunisation against diphtheria.

4.2 DOSE AND METHOD OF ADMINISTRATION

Menactra should be administered as a single 0.5 mL injection by the **intramuscular** route, preferably in the anterolateral thigh or deltoid region depending on the recipient's age and muscle mass.

Primary Vaccination

- In children 9 through 23 months of age, Menactra is given as a 2-dose series 3 months apart.
- Individuals 2 through 55 years of age receive a single dose.

Booster Vaccination

Menactra can also be used for booster vaccination in accordance with the national recommendation. For further information, refer to the current Immunisation Handbook.

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.

For further information, refer to the current 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 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.

4.3 CONTRAINDICATIONS

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

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

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

Guillain-Barré Syndrome

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

GBS has been reported in temporal relationship following administration of Menactra. The risk of GBS following Menactra vaccination was evaluated in a post-marketing retrospective cohort study (see Section 4.8).

Prior to Vaccination

Febrile or Acute Disease

Vaccination must be postponed in case of acute severe febrile disease. However, a minor febrile or non-febrile illness (e.g., a cold) is not usually a reason to postpone immunisation.

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 (epinephrine) 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 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

The immunogenicity of Menactra could be reduced by immunosuppressive treatment. In such cases it is recommended to postpone the vaccination until the end of the immunosuppression.

Menactra has been evaluated in about 300 Human Immunodeficiency Virus (HIV)-infected subjects. Menactra was safe and immunogenic in this population.

Protection

Menactra may not protect 100% of individuals.

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

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

Use in the Elderly

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

Paediatric Use

Menactra is approved for use in children from 9 months of age.

Effects on Laboratory Tests

Interference of Menactra with laboratory tests has not been studied.

4.5 INTERACTION WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTION

For information regarding concomitant administration of Menactra with other vaccines, see Sections 4.8 and 5.1.

If the vaccine is used in individuals under immunosuppressive therapy 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.

4.6 FERTILITY, PREGNANCY AND LACTATION

Pregnancy (Category B1)

In female mice intramuscularly injected with Menactra (at one fifth of the clinical dose per animal or at least 60 times the clinical dose on a mg/kg body weight basis) two weeks prior to mating and on gestation days 6 and 18, no maternal toxicity or effects on embryofetal and postnatal development were observed. However, no Sanofi Pasteur sponsored clinical trials with the primary objective of evaluating Menactra vaccine in pregnant women have been performed and spontaneously reported post-marketing data on the use of this vaccine in pregnant women are limited. 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 Menactra pregnancy registry to prospectively collect data from healthcare providers of patients who received Menactra during pregnancy. The objective of this pregnancy registry is to collect and analyse the outcome of exposure to Menactra during pregnancy and monitor for any potential safety signals that may arise in this population. To date, no safety concern for maternal or infant's health has been identified from this passive surveillance system. The experience with Menactra exposure during pregnancy, however, remains limited.

Healthcare providers are encouraged to inform sanofi pasteur of any pregnant women who receive Menactra for their inclusion in the vaccination pregnancy registry by calling 1800 818 806 (in Australia) or 0800 283 684 (in New Zealand).

Breast-feeding

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 to a nursing woman.

Fertility

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

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

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

4.8 UNDESIRABLE 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.

Children 9 Through 18 Months of Age

The safety of Menactra was evaluated in 4 clinical studies that enrolled approximately 3,700 infants 9-18 months of age. At 12 months of age these children also received one or more other recommended vaccines [MMRV or MMR and Varicella Virus Vaccine Live (V), PCV7, Hepatitis A Vaccine (HepA)]. A control group of 997 children was enrolled at 12 months of age and received two or more childhood vaccines [MMRV (or MMR + V), PCV7, HepA] at 12 months of age (see Section 5.1).

The primary safety study was a controlled trial that enrolled 1256 children who received Menactra at 9 and 12 months of age. At 12 months of age these children received MMRV (or MMR + V), PCV7 and HepA.

Individuals 2 Through 55 years of Age

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

Solicited Adverse Events in the Primary Safety Studies

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

The most frequently reported solicited local and systemic adverse reactions in children aged 2–10 years (Table 2) 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 3), and adults, ages 18-55 years (Table 4) 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 1 - Percentage of US Participants Reporting Solicited Adverse Reactions Within 7 Days Following Vaccine Administration at 9 Months and 12 Months of Age

	Menactra at 9 months of age N[d]=998 - 1002			Menactra + PCV7[a]+ MMRV[b] + HepA[c] vaccines at 12 months of age N[d]=898 - 908			PCV7[a]+ MMRV[b]+ HepA[c] vaccines at 12 months of age N[d]=302 - 307		
Reaction	**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

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

[b] MMRV (ProQuad®) = Measles, Mumps, Rubella and Varicella Virus Vaccine Live

[c] HepA (VAQTA®) = Hepatitis A Vaccine, Inactivated

[d] N = The number of subjects with available data.

[e] Grade 2: cries and protests when injection site is touched, Grade 3: cries when injected limb is moved, or the movement of the injected limb is reduced.

[f] Grade 2: ≥1.0 inches to <2.0 inches, Grade 3: ≥2.0 inches.

[g] Grade 2: requires increased attention, Grade 3: inconsolable.

[h] Grade 2: 1 to 3 hours, Grade 3: >3 hours.

[i] Grade 2: not interested in surroundings or did not wake up for a feed/meal, Grade 3: sleeping most of the time or difficult to wake up.

[j] Grade 2: missed 1 or 2 feeds/meals completely, Grade 3: refuses ≥3 feeds/meals or refuses most feeds/meals.

[k] Grade 2: 2 to 5 episodes per 24 hours, Grade 3: ≥6 episodes per 24 hours or requiring parenteral hydration.

[I] Grade 2: >38.5°C to ≤39.5°C, Grade 3: >39.5°C.

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

	Menactra *N=1157			Menomune–A/C/Y/W-135 *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 3 - Percentage of Participants 11–18 Years of Age Reporting Solicited Adverse Reactions Within 7 Days Following Vaccine Administration

	Menactra N*=2264			Menomune–A/C/Y/W-135 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 ρ < 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 4 - Percentage of Participants 18–55 Years of Age Reporting Solicited Adverse Reactions Within 7 Days Following Vaccine Administration

	Menactra N*=1371			Menomune–A/C/Y/W-135 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 ρ < 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.

Booster Vaccination

The safety of a booster dose of Menactra was evaluated in an open-label, multi-centre trial that enrolled 834 participants to receive a single dose of Menactra 4-6 years after a primary dose. The mean age of participants was 17.8 years (range: 15.0-53.7 years).

Booster vaccination with Menactra was generally safe and well tolerated among adolescents and young adults.

Overall rates of solicited injection-site reactions and solicited systemic reactions were similar to those observed in clinical trials that evaluated primary vaccination in adolescents and adults. The most common solicited injection-site and systemic reactions following booster vaccination were pain and myalgia.

Adverse Events in Concomitant Vaccine Studies

Local and Systemic Reactions when Given with Routine Paediatric Vaccines

In the primary safety study, 1378 US children were enrolled to receive Menactra alone at 9 months of age and Menactra plus one or more other routinely administered vaccines (MMRV, PCV7 and HepA) at 12 months of age (N=961). Another group of children received two or more routinely administered vaccines (MMRV, PCV7 and HepA vaccines) (control group, n=321) at 12 months of age. The frequency of occurrence of solicited adverse events is presented in Table 1.

Local and Systemic Reactions when Given with DTPa Vaccine

In a clinical trial conducted in children 4 to 6 years of age, rates of local and systemic reactions were evaluated after administration of Menactra and DTpa. Menactra and DTPa had similar safety profiles and were well tolerated when administered concomitantly or separately.

Local and Systemic Reactions when Given with dTpa Vaccine

In a clinical trial conducted in adolescents 11 to 17 years of age, Tetanus Toxoid, reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (dTpa) and Menactra had similar safety profiles and were well tolerated when administered concomitantly or separately.

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 was administered 28 days after Td. In both groups, the most common reactions were headache and fatigue.

Local and Systemic Reactions when Given with HPV Vaccine

Concomitant administration of Menactra with HPV vaccines has been evaluated in two studies. In both studies, the safety profiles of the vaccines following concomitant administration were similar to those observed when the vaccines were given separately.

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.

Adverse Reactions from Post-Marketing Surveillance

Based on spontaneous reporting, the following additional adverse events have been reported during the commercial use of Menactra. These events have been very rarely reported, however as exact incidence rates cannot be calculated precisely, their frequency is qualified as “Not known”.

<u>Blood and lymphatic system disorders:</u>

Lymphadenopathy

Immune system disorders:

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

Nervous system disorders:

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

Musculoskeletal and connective tissue disorders:

Myalgia

General disorders and administrative site conditions:

Large injection site reactions, including extensive limb swelling have been reported. These reactions may be associated with erythema, warmth, tenderness or pain at the injection site.

Post-marketing Safety Study

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

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems (Australia) or https://nzphvc.otago.ac.nz/reporting/ (New Zealand).

4.9 OVERDOSE

No case of overdose has been reported.

For general advice on overdose management, contact the Poisons Information Centre, telephone number 13 11 26 (Australia) or the National Poisons Centre, 0800 POISON or 0800 764 766 (New Zealand).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: meningococcal vaccine, ATC code: J07AH08

Mechanism of action

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

Clinical Trials

Immunogenicity

The immunogenicity of Menactra has been studied in three clinical trials in infants 9 through 18 months of age, in four clinical trials among children 2 through 10 years of age, and in six clinical trials among adolescents and adults 11 through 55 years of age.

Menactra induces the production of antibodies specific to the capsular polysaccharides of all vaccine serogroups (A, C, Y and W-135), which are capable of killing the corresponding bacteria. Immunogenicity was assessed by measuring these functional antibodies in a serum bactericidal assay (SBA) using baby rabbit (SBA-BR) or human (SBA-HC) serum as the complement source.

The response to vaccination following one or two doses of vaccine administered to children 9 through 18 months of age and following one dose of vaccine administered to children 2 through 10 years of age was evaluated by the proportion of subjects having an SBA-HC 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 of Menactra has been studied in three clinical trials in approximately 2250 infants 9 through 18 months of age where one or two doses were administered either alone or with concomitant paediatric vaccine(s) (Measles, Mumps, Rubella and Varicella Virus vaccine Live [MMRV] or Pneumococcal 7-valent Conjugate (Diphtheria CRM197 Protein) vaccine [PCV7). A subset of the participants in these trials received Menactra concomitantly with MMRV + *Haemophilus Influenza* type b vaccine [Hib].

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 (N=2526) or Menomune–A/C/Y/W-135 (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 9 through 23 Months of Age

In a primary study (MTA44), the majority of the participants in groups that received the second dose of Menactra alone or with concomitant paediatric vaccines achieved SBA-HC titres ≥1:8 for all serogroups. Groups that received the second dose of Menactra alone had ≥ 91% of subjects achieving an SBA-HC titre ≥1:8 for serogroups A, C, and Y, and ≥86% for serogroup W 135 (Table 5). When the second dose of Menactra was given concomitantly with MMRV (or MMRV+Hib) or with PCV7, the percentages of subjects with SBA-HC titres ≥1:8 were high (>90% for serogroups A, C and Y, and >81% for serogroup W 135). SBA HC GMTs were high for all serogroups.

Table 5 - Proportions of Subjects With SBA HC Antibody Titres ≥ 1:8 and SBA-HC Geometric Mean Titres After the 12 Month Menactra Vaccination, by Study (Per-Protocol Population)

		Group 1 Menactra at 9 months and 12 months (M[a] =272–277) [1]	Group 2 Menactra at 9 months and Menactra + MMRV at 12 months (M[a]=177–180) [1]	Group 3 Menactra at 9 months and Menactra + PCV7 at 12 months (M[a]=264–267) [1]
		% or GMT	% or GMT	% or GMT
% of subjects with titre ≥1:8	A	95.6	92.7	90.5
	C	100.0	98.9	97.8
	Y	96.4	96.6	95.1
	W-135	86.4	88.2	81.2
GMT	A	54.9	52.0	41.0
	C	141.8	161.9	109.5
	Y	52.4	60.2	39.9
	W-135	24.3	27.9	17.9

[a] [1] M: number of subjects in the per-protocol population with valid test results. M varies as indicated depending on the evaluation criterion being considered. Percentages are based on M.

Administration of Menactra to toddlers at 12 months and 15 months of age (N=65) was evaluated in a US study. Prior to the first dose, 33.3% of participants had an SBA-HC titre ≥1:8 to Serogroup A, and 0-2% to serogroups C, Y and W-135. After the second dose, percentages of participants with an SBA-HC titre ≥1:8 were: 85.2%, serogroup A; 100.0%, serogroup C; 96.3%, serogroup Y; 96.2%, serogroup W-135.

In the same study, a group of infants received Menactra at 9 months and 15 months of age (N=65). Prior to the first dose 43.9% of participants had an SBA-HC titre ≥1:8 to serogroup A, and 0-2.2% to serogroups C, Y and W135. After the second dose, percentages of participants with an SBA-HC titre ≥1:8 were: 89.4%, serogroup A; 100.0%, serogroup C; 94.0%, serogroup Y; 92.0%, serogroup W-135.

In MTA26, a Phase II, dose schedule-optimisation study, after a first dose of Menactra given at 9 or 12 months of age in Groups 1, 2 and 3, the percentage of subjects achieving SBA-HC titres ≥ 8 ranged from 51.9% to 75.8% for serogroup A, from 82.9% to 85.4% for serogroup C, from 20.6% to 34.6% for serogroup Y, and from 17.6% to 26.7% for serogroup W-135.

After the second dose of Menactra given at 12 or 15 months, the percentage of subjects in each group achieving titres ≥ 8 ranged from 85.2% (for serogroup A) to 100% (for serogroup C) (Table 6).

Table 6 - Percentage of Subjects with SBA-HC Antibody Titres ≥ 8 (Per-Protocol Population)

Serogroup	Timeframe	Group 1 Menactra at 9 months and 12 months % (95% CI[a])	Group 2 Menactra at 9 months and 15 months % (95% CI[a])	Group 3 Menactra at 12 months and 15 months % (95% CI[a])
A	Post Dose 1	75.8 (57.7, 88.9)	66.7 (51.0, 80.0)	51.9 (37.6, 66.0)
	Post Dose 2	88.9 (73.9, 96.9)	89.4 (76.9, 96.5)	85.2 (72.9, 93.4)
C	Post Dose 1	82.9 (66.4, 93.4)	85.4 (72.2, 93.9)	84.6 (71.9, 93.1)
	Post Dose 2	100.0 (90.5, 100.0)	100.0 (92.9, 100.0)	100.0 (93.4, 100.0)
Y	Post Dose 1	20.6 (8.7, 37.9)	24.4 (12.9, 39.5)	34.6 (22.0, 49.1)
	Post Dose 2	94.6 (81.8, 99.3)	94.0 (83.5, 98.7)	96.3 (87.3, 99.5)
W-135	Post Dose 1	23.5 (10.7, 41.2)	26.7 (14.6, 41.9)	17.6 (8.4, 30.9)
	Post Dose 2	91.7 (77.5, 98.2)	92.0 (80.8, 97.8)	96.2 (86.8, 99.5)

[a] The 95% CI was calculated using the Exact method

This study also evaluated a single dose of Menactra at 15 months or 18 months of age. After a single dose of Menactra at 15 or 18 months, responses for serogroups A and C were similar to those in Groups 1, 2 and 3 after the first dose of Menactra. Responses after the single dose of Menactra at 15 or 18 months for serogroups Y and W-135 were higher than those after a single dose of Menactra at 9 months. However, overall the results confirmed that 2 doses of Menactra are preferred to elicit a high immune response for all 4 serogroups in subjects aged 9 through 15 months.

Immunogenicity in Children 2 through 10 Years of Age

Of 1408 enrolled children 2-10 years old, immune responses evaluated in a subset of Menactra participants (2–3 years old, n=52; 4–10 years old, n=84) and Menomune–A/C/Y/W-135 participants (2–3 years old, n=53; 4–10 years old, n=84) were comparable for all four serogroups (Table 7 and Table 8).

Table 7 - Comparison of Bactericidal Antibody Responses* to Menactra and Menomune–A/C/Y/W-135 28 Days After Vaccination for a Subset of Participants Aged 2–3 Years

		Menactra N‡=48-52		Menomune–A/C/Y/W-135 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 8 - Comparison of Bactericidal Antibody Responses* to Menactra and Menomune–A/C/Y/W-135 28 Days After Vaccination for a subset of Participants Aged 4–10 Years

		Menactra N‡=84		Menomune–A/C/Y/W-135 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 and Menomune–A/C/Y/W-135 recipients. Menactra 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 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 and Menomune–A/C/Y/W-135 recipients. Menactra 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 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 11 through 18 years of Age

Results from the comparative clinical trial conducted in 881 adolescents aged 11-18 years showed that the immune responses to Menactra and Menomune–A/C/Y/W-135 were similar for all four serogroups (Table 9).

Table 9 - Comparison of Bactericidal Antibody Responses* to Menactra and Menomune–A/C/Y/W-135 28 Days after Vaccination for Participants Aged 11–18 Years

		Menactra N‡=423		Menomune–A/C/Y/W-135 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 was non-inferior to Menomune–A/C/Y/W-135. 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 and Menomune–A/C/Y/W-135 recipients. Menactra 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 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 Adolescents and Adults following Booster Vaccination

In an open-label, multi-centre trial conducted in the US (MTA77), 834 participants < 56 years of age were enrolled to receive a single dose of Menactra 4-6 years after a primary dose at ≥ 11 years of age. The mean age of subjects was 17.8 years. The rapidity and magnitude of the anti-meningococcal antibody increases following booster vaccination with Menactra suggested these were anamnestic responses.

Among the randomly chosen subset of trial participants for whom immune responses at Day 6 were assessed (n=112), 86.6%, 91.1%, 94.6%, and 92.0% achieved ≥4-fold rises in SBA-H antibody titres for Serogroups A, C, Y, and W-135, respectively. The proportions of participants (n=781) who achieved ≥4-fold rises in SBA-H antibody titres by Day 28 were 95.0%, 95.3%, 97.1%, and 96% for Serogroups A, C, Y, and W-135, respectively. The proportions of participants who achieved an SBA-H titre ≥1:8 by Day 28 were >99% for each serogroup.

Immunogenicity in Adults 18 through 55 years of Age

Results from the comparative clinical trial conducted in 2554 adults aged 18-55 years showed that the immune responses to Menactra and Menomune–A/C/Y/W-135 were similar for all four serogroups (Table 10).

Table 10 - Comparison of Bactericidal Antibody Responses* to Menactra and Menomune–A/C/Y/W-135 28 Days After Vaccination for Participants Aged 18–55 Years

		Menactra N‡=1280		Menomune–A/C/Y/W-135 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 was non-inferior to Menomune–A/C/Y/W-135. 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 and Menomune–A/C/Y/W-135 recipients. Menactra 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 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

PCV7, MMR, V, MMRV, HepA, Hib

In clinical trials conducted in children younger than 2 years of age, Pneumococcal 7-valent Conjugate Vaccine (PCV7), Measles, Mumps, and Rubella Virus Vaccine (MMR), Varicella Virus Vaccine Live (V), Measles, Mumps, Rubella and Varicella Virus Vaccine Live (MMRV), Hepatitis A Vaccine (HepA) or Haemophilus influenzae type b Vaccine (Hib) were co-administered with the second dose of Menactra at 12 months of age. Menactra and all these vaccines had similar safety profiles when administered concomitantly or separately at 12 months of age. The immunogenicity profiles of Menactra and MMRV, MMR+V, or Hib were also similar when these vaccines were given concomitantly or separately.

When Menactra was administered concomitantly with PCV, antibody responses to 3 of the 7 serotypes in PCV (MTA37) and to serogroup W-135 (MTA44) of Menactra did not meet the non-inferiority criteria. Given the high antibody response rates to all PCV serotypes when assessed by either ELISA or OPA, and considering that >81% of subjects achieved SBA-HC antibody titres ≥1:8 for all 4 serogroups of Menactra, it is unlikely that there will be any impact on the clinical efficacy of either of these vaccines when administered concomitantly.

Diphtheria, Tetanus and Acellular Pertussis

The concomitant use of Menactra and Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed (DTPa) was evaluated in a double-blind, randomised clinical trial (MTA43) conducted in 881 participants aged 4-6 years.

When Menactra as administered 30 days after DTPa (and Inactivated Polio Vaccine (IPV)) [Group 1], significantly lower SBA-HC GMTs to all 4 meningococcal serogroups were observed compared to Menactra (and IPV) administered 30 days prior to DTPa [Group 3]. When Menactra was administered concomitantly with DTPa [Group 2], SBA-HC GMTs to meningococcal serogroups A, C, and W-135 were non-inferior to those observed after Menactra (and IPV) [Group 3]. The non-inferiority criterion was marginally missed for meningococcal serogroup Y. Non-inferiority of SBA-HC GMTs following concomitant administration of Menactra and DTPa compared to those after concomitant Menactra and IPV was concluded if the upper limit of the 2-sided 95% CI of (GMTGroupC divided by GMTGroupB) computed separately for each of the serogroup was < 2.

Table 11 - Bacterial Antibody Responses* 30 days Following Menactra Administered Alone or Concomitantly with DTPa or IPV

		Vaccines administered at Visit 1 and 30 days later at Visit 2					
		Group 1		Group 2		Group 3	
	Visit 1	DTPa +IPV		Menactra +DTPa		Menactra + IPV	
	Visit 2	Menactra		IPV		DTPa	
		N‡=250		N‡=238		N‡=121	
Serogroup			(95% CI)§		(95% CI)§		(95% CI)§
A	% ≥ 1:8†	49.6	(41.0; 58.3)	67.2	(58.4; 75.1)	64.4	(54.4; 73.6)
	GMT	6.7	(5.7; 8.0)	10.8	(8.7; 13.3)	10.4	(8.1; 13.3)
C	% ≥ 1:8†	20.3	(13.9; 28.0)	50.4	(41.5; 59.2)	50.5	(40.5; 60.5)
	GMT	3.3	(2.7; 3.9)	8.1	(6.3; 10.5)	7.8	(5.8; 10.7)
Y	% ≥ 1:8†	44.2	(35.8; 52.9)	80.2	(72.3; 86.6)	88.5	(80.7; 93.9)
	GMT	6.5	(5.1; 8.2)	18.1	(14.2; 22.9)	26.2	(20.0; 34.4)
W-135	% ≥ 1:8†	55.1	(46.4; 63.5)	87.8	(80.9; 92.9)	82.7	(74.0; 89.4)
	GMT	8.4	(6.7; 10.6)	22.8	(18.5; 28.1)	21.7	(16.6; 28.4)

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

† The proportion of participants achieving an SBA-HC titre of at least 1:8, 30 days after Menactra.

‡ N = Total number of the subjects in the study population per group.

§ 95% CI for the proportions are calculated based on the Clopper-Pearson Exact method and normal approximation for that of the GMTs.

Significantly lower antibody responses to all 4 meningococcal serogroups were observed when Menactra was administered 1 month after DTPa. As a measure of precaution, in cases where Menactra and DTPa vaccine are to be administered at 4 through 6 years of age, preference should be given to simultaneous administration of the 2 vaccines or administration of Menactra prior to DTPa vaccine.

Tetanus, reduced Diphtheria and Acellular Pertussis

The concomitant use of Menactra and Tetanus Toxoid, reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (dTpa) and Menactra was evaluated in a clinical trial conducted in adolescents 11 to 17 years of age. The concomitant administration of dTpa and Menactra induced antibody responses to all 4 meningococcal serogroups A, C, Y, and W-135 that were non-inferior to those observed when Menactra was administered separately.

Tetanus and Diphtheria

The concomitant use of Menactra 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 was given concomitantly with Td than when Menactra 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.

Human Papillomavirus

Concomitant administration of Menactra with HPV vaccines has been evaluated in two studies. In one study, Menactra was co-administered with human papillomavirus bivalent (Types 16 and 18) AS04-adjuvanted vaccine (HPV2) alone and with Tdap to females 11 – 18 years of age. In another study, Menactra was co-administered with both human papillomavirus quadrivalent (Types 6, 11, 16 and 18) vaccine (HPV4) and dTpa to females and males 10 – 17 years of age. Concomitant administration of Menactra and dTpa with HPV did not interfere with the immune responses to any antigens in these vaccines.

Typhoid Vi Polysaccharide Vaccine, Typhim Vi®

The concomitant use of Menactra and Typhim Vi (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 and to Typhim Vi when given concurrently was comparable to the immune response when Menactra or Typhim Vi was given alone.

5.2 PHARMACOKINETIC PROPERTIES

No pharmacokinetic studies have been performed.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No genotoxicity studies have been conducted with Menactra.

Carcinogenicity

No carcinogenicity studies have been conducted with Menactra.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

- Sodium chloride 4.35 mg
  (within 0.85% Physiological Saline[†] and 0.5M Phosphate Buffered Saline[§], pH 6.8)
- Dibasic sodium phosphate 0.348 mg
  (within 0.5M Phosphate Buffered Saline[§], pH 6.8)
- Monobasic sodium phosphate 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, dibasic sodium phosphate and monobasic sodium phosphate in Water for Injections.

6.2 INCOMPATIBILITIES

Menactra must not be mixed with any vaccine in the same syringe.

6.3 SHELF LIFE

24 months.

6.4 SPECIAL PRECAUTIONS FOR 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.

6.5 NATURE AND CONTENTS OF CONTAINER

Vial, 1 Dose

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

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7 MEDICINE SCHEDULE

Prescription

8 SPONSOR

Australia:

sanofi-aventis australia pty ltd
Talavera Corporate Centre - Building D
12-24 Talavera Road
Macquarie Park NSW 2113
Australia

Tel: 1800 818 806

New Zealand:

sanofi-aventis new zealand pty ltd
Level 8,
56 Cawley St
Ellerslie
Auckland
New Zealand

Tel: 0800 283 684

9 DATE OF FIRST APPROVAL

08 March 2012

10 DATE OF REVISION OF THE TEXT

05 July 2018

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
All	Reformat of Data sheet including addition of text to align with requirements.
4.2	Addition of booster vaccination in accordance with the national recommendation.
4.3	Removal of febrile or acute disease contraindications.
4.4	Update to protection and febrile or acute disease precautions.
4.6	Update to use in pregnancy.
4.8	Addition of safety data following booster and co-administration with other vaccines. Addition of new safety data from post-marketing surveillance.
5.1	Addition of immunogenicity data in children 9-23 months of age, immunogenicity in adolescents/adults following booster and co-administration with other vaccines.