PRODUCT MONOGRAPH

NIMENRIX®

Meningococcal polysaccharide groups A, C, W-135 and Y conjugate vaccine

Powder and diluent for solution for injection

Active Immunizing Agent

Pfizer Canada Inc.
17,300 Trans-Canada Highway
Kirkland, Quebec H9J 2M5

Date of Revision:
February 29, 2016

Submission Control No: 184020

Date Approved: March 23, 2016

Table of Contents

NIMENRIX®

Meningococcal polysaccharide groups A, C, W-135 and Y conjugate vaccine

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
Intramuscular Injection	Powder and diluent for solution for injection/ *Neisseria meningitidis* serogroup A polysaccharide[1] 5 micrograms *Neisseria meningitidis* serogroup C polysaccharide[1] 5 micrograms *Neisseria meningitidis* serogroup W-135 polysaccharide[1] 5 micrograms *Neisseria meningitidis* serogroup Y polysaccharide[1] 5 micrograms	Sucrose Trometamol Sodium chloride *For a complete listing see Dosage Forms, Composition and Packaging section.*

[1] conjugated to tetanus toxoid carrier protein 44 micrograms

DESCRIPTION

NIMENRIX® (meningococcal polysaccharide groups A, C, W-135 and Y conjugate vaccine) is a tetravalent meningococcal polysaccharide conjugated vaccine consisting of *Neisseria meningitidis* capsular polysaccharides A, C, W-135 and Y each coupled to tetanus toxoid as a carrier protein. The *Neisseria meningitidis* serogroups A and C polysaccharides are conjugated with an adipic dihydrazide (AH) spacer and indirectly conjugated to the tetanus toxoid whereas the W-135 and Y polysaccharides are conjugated directly to tetanus toxoid.

The vaccine does not contain any preservatives or adjuvants.

INDICATIONS AND CLINICAL USE

NIMENRIX® is indicated for the active immunization of individuals from 12 months to 55 years of age against invasive meningococcal diseases caused by *Neisseria meningitidis* serogroups A, C, W-135 and Y.

CONTRAINDICATIONS

NIMENRIX® should not be administered to subjects with known hypersensitivity to any component of the vaccine. For a complete listing, see the DOSAGE FORMS, COMPOSITION AND PACKAGING section.

WARNINGS AND PRECAUTIONS

General

NIMENRIX® should under no circumstances be administered intravascularly, intradermally or subcutaneously.

It is good clinical practice to precede vaccination by a review of the medical history (especially with regard to previous vaccination and possible occurrence of undesirable effects) and a clinical examination.

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of the vaccine.

Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. It is important that procedures are in place to avoid injury from faints.

NIMENRIX® will only confer protection against *Neisseria meningitidis* serogroups A, C, W-135 and Y. The vaccine will not protect against other *Neisseria meningitidis* serogroups.

Although NIMENRIX® contains tetanus toxoid, this vaccine does not substitute for tetanus immunization.

In toddlers, persistence of antibodies has been evaluated for up to 5 years after vaccination. Similar to the monovalent Men C comparator (Meningitec®), a decline in antibody titres over time has been observed. Although the clinical relevance of the waning antibody titres is unknown, in individuals vaccinated as toddlers and remaining at high risk of exposure to meningococcal disease caused by serogroups A, C, W-135 and Y, a booster dose might be considered (see CLINICAL TRIALS).

A more rapid waning of serum bactericidal antibody titres against MenA than for other serogroups (C, W-135, Y) has been observed when using human complement in the assay (see CLINICAL TRIALS). In individuals expected to be at particular risk of exposure to MenA and

who received a first dose of NIMENRIX® more than one year earlier, consideration may be given to administering a booster dose of NIMENRIX®. Available data indicate that a booster dose will elicit an anamnestic immune response to all four meningococcal serogroups in the vaccine. Currently there is very limited information available on the safety of a booster dose of NIMENRIX®.

Febrile Illness

As with other vaccines, vaccination with NIMENRIX® should be postponed in subjects suffering from an acute severe febrile illness. The presence of a minor infection, such as a cold, should not result in the deferral of vaccination.

Hematologic

As with other vaccines administered intramuscularly, NIMENRIX® should be given with caution to individuals with thrombocytopenia or any coagulation disorder since bleeding may occur following an intramuscular administration to these subjects.

Immune

As with any vaccine, a protective immune response may not be elicited in all vaccinees.

It may be expected that in patients receiving immunosuppressive treatment or patients with immunodeficiency, an adequate immune response may not be elicited.

Safety and immunogenicity have not been assessed in patients with increased susceptibility to meningococcal infection due to conditions such as terminal complement deficiencies and anatomic or functional asplenia. In these individuals, an adequate immune response may not be elicited.

Special Populations

Pregnant Women: There is limited experience with use of NIMENRIX® in pregnant women.

Animal studies with NIMENRIX® do not indicate direct or indirect harmful effects with respect to fertility, pregnancy, embryo/fetal development, parturition or post-natal development (see TOXICOLOGY).

NIMENRIX® should be used during pregnancy only when clearly needed, and the possible advantages outweigh the potential risks for the fetus.

Nursing Women: The safety of NIMENRIX® when administered to breastfeeding women has not been evaluated. It is unknown whether NIMENRIX® is excreted in human breast milk.

NIMENRIX® should only be used during breast-feeding when the possible advantages outweigh the potential risks.

Pediatrics: The safety and immunogenicity of NIMENRIX® in children under 12 months of age have not been established

ADVERSE REACTIONS

Adverse Drug Reaction Overview

The safety profile is based on a pooled analysis on 9,621 subjects who have been vaccinated with one dose of NIMENRIX® in clinical studies. The pooled analysis includes data for 3,079 toddlers (12 months to 23 months), 1,899 children (2 to 10 years), 2,317 adolescents (11 to 17 years) and 2,326 adults (18 – 55 years). In addition, a descriptive study provides safety data from 274 individuals aged 56 years and older and who have been vaccinated with one dose of NIMENRIX®.

Clinical Trial Adverse Drug Reactions

Because clinical trials are conducted under very specific conditions the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse drug reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

Solicited Adverse Reactions:

Infants 12 to 23 months old

In Study MenACWY-TT-039, healthy children 12 through 23 months of age were administered one dose of NIMENRIX® either alone or co-administered with a first dose of PRIORIX-TETRA®, 1 dose of PRIORIX-TETRA® or 1 dose of a licensed MenC-CRM$_{197}$ (MenC-CRM) vaccine.

Table 1 presents the rates of solicited symptoms reported during the 4-day post-vaccination period in the Co-administered (Co-ad), NIMENRIX®, PRIORIX-TETRA® and MenC-CRM groups.

Table 1 Study MenACWY-TT-039: Percentage of subjects with solicited local and general symptoms reported during the 4-day (Days 0-3) post-vaccination period (Total vaccinated cohort)

	Type	NIMENRIX® + PRIORIX-TETRA® N=375	NIMENRIX® N=367	PRIORIX-TETRA® N=124	MenC-CRM N=123
Local Symptoms, %					
Pain	All	24.3	29.2	17.7	25.2
	Grade 3	0.3	0.8	0.0	0.0
Redness	All	35.5	37.1	38.7	31.7
	> 30 mm	1.9	4.4	0.0	0.0
Swelling	All	13.9	18.8	5.6	8.1
	> 30 mm	2.4	4.1	0.0	0.0
General Symptoms, %					
	Type	**NIMENRIX® + PRIORIX-TETRA® N=375**	**NIMENRIX® N=367**	**PRIORIX-TETRA® N=124**	**MenC-CRM N=124**
Drowsiness	All	32.5	28.1	23.4	32.3
	Grade 3	0.3	0.0	0.8	0.0
Fever (Rectally)	All (≥38°C)	14.9	9.3	11.3	12.9
	>40°C	0.0	0.0	0.8	0.0
Irritability	All	50.7	40.9	38.7	43.5
	Grade 3	0.8	0.5	1.6	0.0
Loss of appetite	All	28.5	22.9	23.4	26.6
	Grade 3	0.3	0.0	0	0.0

N= number of subjects with the dose documented
%= percentage of subjects reporting the symptom at least once

Redness was the most frequently reported solicited local symptom in each group after each vaccination (38.7% in the PRIORIX-TETRA® group, 35.5% in the Co-ad group and 37.1% in the NIMENRIX® group and 31.7% in the MenC-CRM group).

Irritability was the most frequently reported solicited general symptom in the 4 groups (50.7% in the Co-ad group, 40.9% in the NIMENRIX® group, 38.7% in the PRIORIX-TETRA® group and 43.5% in the MenC-CRM group).

Children (2-10 Years Old), Adolescents (10-25 Years Old), and Adults (18-55 Years Old)

Children (2-5 Years Old)

In Study MenACWY-TT-081, healthy children aged 2 through 10 years of age were administered 1 dose of NIMENRIX® or 1 dose of a licensed MenC-CRM vaccine.

Table 2 presents the percentage of subjects (aged 2 through 5 years of age) with solicited adverse reactions during the 4-day post vaccination period in the NIMENRIX® and MenC-CRM groups.

Table 2 MenACWY-TT-081: Percentage of subjects with solicited local and general symptoms reported during the 4-day (Days 0-3) post-vaccination period (Total vaccinated cohort), subjects 2 through 5 years of age

	Type	NIMENRIX® N=162	MenC-CRM N=53
Local Symptoms, %			
Pain	All	27.8	28.3
	Grade 3	0.0	1.9
Redness	All	35.2	39.6
	>30 mm	6.8	15.1
Swelling	All	26.5	24.5
	>30 mm	4.3	5.7
General Symptoms, %			
Drowsiness	All	14.2	11.3
	Grade 3	0.0	1.9
Fever/(Orally)	All (≥37.5°C)	5.6	5.7
	>39.5°C	0.0	0.0
Irritability	All	15.4	11.3
	Grade 3	0.6	1.9
Loss of Appetite	All	10.5	9.4
	Grade 3	0.0	0.0

N= number of subjects with the dose documented
%= percentage of subjects reporting the symptom at least once

Redness was the most frequently reported solicited local symptom in each group (35.2% and 39.6% of the subjects in the NIMENRIX® group and MenC-CRM group, respectively).

Irritability was the most frequently reported solicited general symptom in each group (15.4% and 11.3% of the subjects in the NIMENRIX® group and MenC-CRM group, respectively). Drowsiness was also reported by 11.3% of the subjects in the MenC-CRM group, as compared to 14.2% of the subjects in the NIMENRIX® group. Fever ≥ 37.5°C was reported by 5.6% of the subjects in the NIMENRIX® group and 5.7% of the subjects in the MenC-CRM. The majority of fevers were measured by the rectal route (66.7% in the NIMENRIX® group and 100% in the MenC-CRM group).

Children aged 6-10 years

Table 3 includes the percentage of subjects (aged 6 through 10 years of age) with solicited adverse reactions during the 4-day post vaccination period in the NIMENRIX® and MenC-CRM groups.

Pain was the most frequently reported solicited local symptom in each group (43.9% and 54.0% of the subjects in the NIMENRIX® group and MenC-CRM group, respectively).

Fatigue was the most frequently reported solicited general symptom in each group (22.3% and 22.0% of the subjects in the NIMENRIX® group and MenC-CRM group, respectively). Fever ≥ 37.5°C was reported in 6.8% of the subjects in the NIMENRIX® group and 2.0% of the subjects in the MenC-CRM group.

Adolescents aged 10-25 years

In Study MenACWY-TT-071, healthy subjects aged 10 through 25 years of age were administered 1 dose of NIMENRIX® or 1 dose of MENACTRA® (ACWY-DT vaccine).

Table 3 includes the percentage of subjects (aged 10 through 25 years of age) with solicited adverse reactions during the 4-day post vaccination period in the NIMENRIX® and MENACTRA® groups.

The most common solicited local symptom during the 4-day post-vaccination period was pain at the injection site, reported by 51.4% and 55.4% of subjects in the NIMENRIX® and MENACTRA® groups, respectively. A much smaller percentage of these subjects reported pain with grade 3 intensity, ranging between 0.6% and 2.4% across all vaccine groups.

The incidence of redness at the injection site was 25.8% and 20.3% of subjects in the NIMENRIX® and MENACTRA® groups, respectively. The incidence of swelling was 19.1% and 13.5% of subjects, respectively. The majority of these events were grade 1 in intensity. Grade 3 events of redness (i.e. > 50 mm in diameter) were reported by 3 and 6 subjects in the NIMENRIX® and MENACTRA® groups, respectively. Grade 3 events of swelling (i.e. > 50 mm in diameter) were reported by 3 subjects each of the two vaccine groups.

The most common solicited general symptom was fatigue with an incidence of 27.3% to 29.2% across the two vaccine groups. Headache was reported by 25.5% to 26.4% and gastrointestinal symptoms by 13.1% to 13.5% of subjects across the two vaccine groups.

Adults aged 18-55 years

In Study MenACWY-TT-035, healthy adults aged 18 through 55 years of age were administered either 1 dose of NIMENRIX®, 1 dose of a licensed ACWY-PS (polysaccharide) vaccine, or 1 dose of NIMENRIX® co-administered with a licensed influenza vaccine, FLUARIX®.

Table 3 includes the percentage of subjects (aged 18 through 55 years of age) with solicited adverse reactions during the 4-day post vaccination period in the NIMENRIX®, ACWY-PS and Co-administered groups.

Pain was the most frequently reported solicited local symptom in each group (19.4% in the NIMENRIX® group, 21.9% in the Co-administered group and 13.5% in the ACWY-PS group). Headache was the most frequently reported solicited general symptom in each group (16.3% in the NIMENRIX® group, 14.2% in the ACWY-PS group, and 13.3% in the Co-administered group).

Table 3 Percentage of subjects with solicited local and general symptoms reported during the 4-day (Days 0-3) post-vaccination period (Total vaccinated cohort), subjects 6 through 55 years of age

		MenACWY-TT-081		MenACWY-TT-071		MenACWY-TT- 035		
Age		**6-10 Years old**		**10-25 Years old**		**18-55 Years old**		
	Type	**NIMENRIX® N=148**	**MenC N=50**	**NIMENRIX® N=329**	**MENACTRA® N=325**	**NIMENRIX® N=927**	**NIMENRIX® + FLUARIX® N=105**	**ACWY-PS N=310**
Local Symptoms, %								
Pain	All	43.9	54.0	51.4	55.4	19.4	21.9	13.5
	Grade 3	2.0	6.0	2.4	0.6	0.4	1.0	0.3
Redness	All	39.2	38.0	25.8	20.3	8.8	5.7	4.5
	>50 mm	6.1	10.0	0.9	1.8	1.3	0.0	0.0
Swelling	All	29.7	30.0	19.1	13.5	7.9	1.0	1.9
	>50 mm	2.7	6.0	0.9	0.9	1.1	0.0	0.0
General Symptoms, %								
	Type	**NIMENRIX® N=148**	**MenC N=50**	**NIMENRIX® N=329**	**MENACTRA® N=326**	**NIMENRIX® N=927**	**NIMENRIX® + FLUARIX® N=105**	**ACWY-PS N=310**
Fatigue	All	22.3	22.0	29.2	27.3	12.3	9.5	9.7
	Grade 3	2.7	0.0	2.7	1.5	0.9	0.0	0.0
Fever	All (≥37.5°C)	6.8	2.0	5.2	4.9	4.0	2.9	4.5
	>39.5°C	0.0	0.0	0.3	0.0	0.2	0.0	0.6
Gastro-intestinal	All	14.9	8.0	13.1	13.5	4.6	1.9	3.2
	Grade 3	0.7	0.0	1.2	1.2	0.2	0.0	0.3
Headache	All	20.3	8.0	26.1	25.5	16.3	13.3	14.2
	Grade 3	1.4	0.0	1.5	1.8	1.5	0.0	1.6

N= number of subjects with the dose documented
%= percentage of subjects reporting the symptom at least once
Study 081 and Study 071: Fever (≥37.5°C) (Orally)
Study 035: Fever (≥37.5°C) (Axillary)

Adults aged > 55 years

In a descriptive study a single dose of NIMENRIX® was administered to 274 individuals aged 56 years and older. The adverse reactions reported in this study were already observed in younger age groups.

Common and Uncommon Clinical Trial Adverse Drug Reactions

Adverse reactions reported during clinical studies included in the safety pooled analysis:

Common (≥ 1% to < 10%): Injection site hematoma

Uncommon (≥ 0.1% to < 1%): insomnia, crying, hypoesthesia, dizziness, pruritus, rash, myalgia, pain in extremity, malaise, and injection site reaction (including induration, pruritus, warmth, anesthesia).

Post-Market Adverse Drug Reactions

General disorders and administration site conditions
Rare (≥ 1/10,000 and <1/1000): extensive limb swelling at the injection site, frequently associated with erythema, sometimes involving the adjacent joint or swelling of the entire injected limb.

DRUG INTERACTIONS

Drug Interactions

NIMENRIX® can be given concomitantly with any of the following vaccines: hepatitis A and hepatitis B vaccines (HAV and HBV), measles-mumps-rubella vaccine (MMR), measles-mumps-rubella-varicella vaccine (MMRV), 10-valent pneumococcal conjugate vaccine or unadjuvanted seasonal influenza vaccine.

NIMENRIX® can also be given concomitantly with combined diphtheria-tetanus-acellular pertussis vaccines in the second year of life, including combination DTPa vaccines with hepatitis B, inactivated polio or *Haemophilus influenzae* type b, such as DTPa-HBV-IPV/Hib vaccine.

Safety and immunogenicity of NIMENRIX® was evaluated when sequentially administered or co-administered with a DTPa-HBV-IPV/Hib vaccine in the second year of life. The administration of NIMENRIX® one month after the DTPa-HBV-IPV/Hib vaccine resulted in lower MenA, MenC and MenW-135 rSBA GMTs. Clinical relevance of this observation is unknown, since at least 99.4% of subjects (N=178) had rSBA titres ≥ 8 for each group (A, C, W-135, Y). Whenever possible, NIMENRIX™ and a tetanus toxoid (TT) containing vaccine, such as DTPa-HBV-IPV/Hib vaccine, should be co-administered or NIMENRIX® should be administered at least one month before the TT-containing vaccine.

One month after co-administration with a 10-valent pneumococcal conjugate vaccine, lower Geometric Mean antibody Concentrations (GMCs) and opsonophagocytic assay (OPA) antibody GMTs were observed for one pneumococcal serotype (18C conjugated to tetanus toxoid carrier protein). Clinical relevance of this observation is unknown. There was no impact of co-administration on the other nine pneumococcal serotypes.

If NIMENRIX® is to be given at the same time as another injectable vaccine, the vaccines should always be administered at different injection sites.

Use with systemic immunosuppressive medications
As with other vaccines, it may be expected that in patients receiving immunosuppressive treatment, an adequate response may not be elicited.

DOSAGE AND ADMINISTRATION

Dosing Considerations
NIMENRIX® should be used in accordance with available official recommendations.

Recommended Dose and Dosage Adjustment
Primary vaccination
A single 0.5 mL dose of the reconstituted vaccine is used for immunization.

Booster vaccination
There are no data available in subjects previously vaccinated with a meningococcal C conjugate vaccine.

NIMENRIX® may be given in subjects who have previously been vaccinated with a plain polysaccharide meningococcal vaccine (see CLINICAL TRIALS).

Administration
NIMENRIX® is for intramuscular injection only, preferably in the deltoid muscle.

In children 12 to 23 months of age, NIMENRIX® may also be administered in the anterolateral part of the thigh (see WARNINGS AND PRECAUTIONS and DRUG INTERACTIONS).

For instructions on reconstitution of the vaccine before administration, see SPECIAL HANDLING INSTRUCTIONS.

The reconstituted vaccine is a clear colourless solution.

The reconstituted vaccine should be inspected visually for any foreign particulate matter and/or variation of physical aspect prior to administration. In the event of either being observed, discard the vaccine.

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

OVERDOSAGE

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

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

Anti-capsular meningococcal antibodies protect against meningococcal diseases via complement mediated bactericidal killing. NIMENRIX® induces the production of bactericidal antibodies against capsular polysaccharides of serogroups A, C, W-135 and Y when measured by assays using either rabbit complement (rSBA) or human complement (hSBA). By conjugating capsular polysaccharide to a protein carrier that contains T-cell epitopes, meningococcal conjugate vaccines like NIMENRIX® change the nature of immune response to capsular polysaccharide from T-cell independent to T-cell dependent.

Canadian epidemiological data is available on the Public Health Agency of Canada website: http://www.phac-aspc.gc.ca/im/vpd-mev/meningococcal-eng.php.

STORAGE AND STABILITY

Store in a refrigerator (2°C – 8°C). The diluent may also be stored at ambient temperature (25°C).

Do not freeze. Protect from light.

For shelf-life after reconstitution of the vaccine, see SPECIAL HANDLING INSTRUCTIONS.

SPECIAL HANDLING INSTRUCTIONS

In the absence of compatibility studies, NIMENRIX® must not be mixed with other medicinal products.

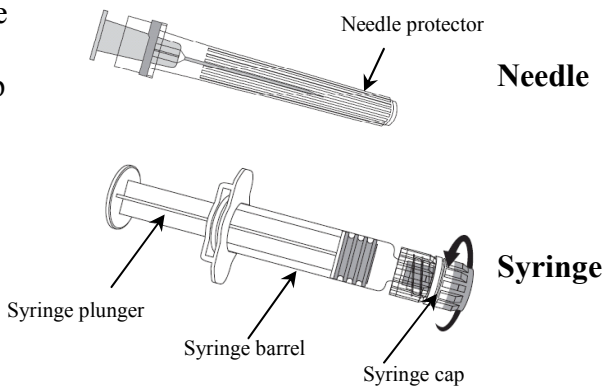
Instructions for reconstitution of the vaccine with the diluent presented in pre-filled syringe

NIMENRIX® must be reconstituted by adding the entire content of the pre-filled syringe of diluent to the vial containing the powder.

To attach the needle to the syringe, refer to the below drawing.

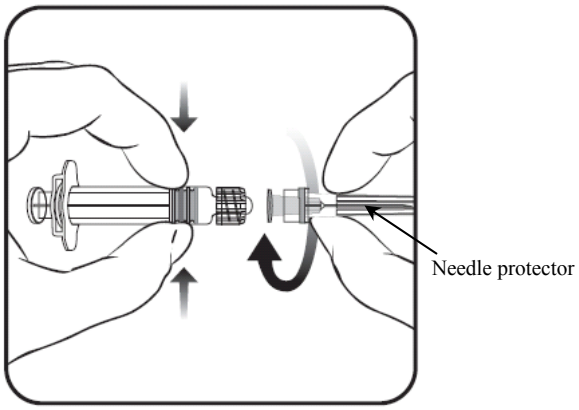
Note: However, the syringe provided with NIMENRIX® might be slightly different (without screw thread) than the syringe described in the drawing. In that case, the needle should be attached without screwing.

1. Holding the syringe **barrel** in one hand (avoid holding the syringe plunger), unscrew the syringe cap by twisting it anticlockwise.



2. To attach the needle to the syringe, twist the needle clockwise into the syringe until you feel it lock (see drawing).

3. Remove the needle protector, which on occasion can be a little stiff.



4. Add the diluent to the powder. After the addition of the diluent to the powder, the mixture should be well shaken until the powder is completely dissolved in the diluent.

After reconstitution, the vaccine should be used promptly. Although delay is not recommended, stability has been demonstrated for 8 hours at 30°C after reconstitution. If not used within 8 hours, do not administer the vaccine.

A new needle should be used to administer the vaccine.

Instructions for reconstitution of the vaccine with diluent presented in ampoules

NIMENRIX® must be reconstituted by adding the entire content of the ampoule of diluent to the vial containing the powder.

To do so, break the top of the ampoule, draw up the diluent with a syringe and add the diluent to the powder.

The mixture should be well shaken until the powder is completely dissolved in the diluent.

After reconstitution, the vaccine should be used promptly. Although delay is not recommended, stability has been demonstrated for 8 hours at 30°C after reconstitution. If not used within 8 hours, do not administer the vaccine.

A new needle should be used to administer the vaccine.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Dosage Form

NIMENRIX® (meningococcal polysaccharide groups A, C, W-135 and Y conjugate vaccine) is supplied as a sterile lyophilized white powder in a single dose vial.

The diluent (sodium chloride and water for injections) is a sterile clear and colourless liquid supplied separately in a prefilled syringe or ampoule*.

**Format not available in Canada.*

After reconstitution, NIMENRIX® is a clear colourless solution.

Composition

After reconstitution, 1 dose (0.5 mL) contains:

Active Ingredients

Neisseria meningitidis serogroup A polysaccharide[1]	*5 micrograms*
Neisseria meningitidis serogroup C polysaccharide[1]	*5 micrograms*
Neisseria meningitidis serogroup W-135 polysaccharide[1]	*5 micrograms*
Neisseria meningitidis serogroup Y polysaccharide[1]	*5 micrograms*
[1]conjugated to tetanus toxoid carrier protein	44 micrograms

Excipients

Powder:

Sucrose	28 mg
Trometamol	97 µg

Diluent:

Sodium chloride	4.5 mg
Water for Injections	q.s. to 0.5 mL

Packaging

NIMENRIX® is supplied in a 3 mL single dose glass vial. The diluent (0.5 mL) is supplied in a prefilled syringe or ampoule*.

The vials, syringes, and ampoules* are made of neutral glass Type 1.

NIMENRIX® is available in pack sizes as follows:

- Single dose vial packaged with pre-filled syringe of diluent with or without needles in pack sizes of 1 and 10.
- Single dose vial packaged with ampoule* of diluent in pack sizes of 1, 10 or 100.

**Format not available in Canada.*

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

NIMENRIX® is composed of the purified capsular polysaccharides of *Neisseria meningitidis* serogroups A, C, W-135 and Y, each conjugated to tetanus toxoid.

CLINICAL TRIALS

The immunogenicity of one dose of NIMENRIX® has been evaluated in more than 9,000 subjects aged ≥12 months.

Vaccine efficacy was inferred from the demonstration of immunologic non-inferiority (based mainly on comparing proportions with rabbit complement serum bactericidal assay (rSBA) titres at least 1:8) to licensed meningococcal vaccines. Immunogenicity was measured by using rSBA or human complement serum bactericidal assay (hSBA) which are biomarkers for protective efficacy against meningococcal serogroups A, C, W-135 and Y.

Table 4 Study demographics and trial design

Study #	Study Objectives	Trial design	No. of study subjects[§]	Mean age in Years (Range)	Gender Male/ Female
12-23 months					
Men ACWY-TT -039	Immunogenicity and safety compared to Meningococcal C-CRM$_{197}$ conjugate (MenC-CRM) vaccine and concomitant administration with measles-mumps-rubella-varicella vaccine (MMRV)	Open, randomized, controlled, multi-centre	Total=972 NIMENRIX®=366 Co-admin =361 MMRV=121 MenC-CRM =124	14.6 months (12-19 months)	507/465
2-10 years					
Men ACWY-TT -081	Immunogenicity and safety compared to MenC-CRM	Open, randomized, controlled, multi-centre	Total=395 NIMENRIX®=296 MenC-CRM =99	5.6 (2-10)	191/204
10-55 years					
Men ACWY-TT -035	Lot-to-lot consistency; immunogenicity and safety compared to ACWY-PS and concomitant administration with influenza virus vaccine	Partially double-blinded, randomized, controlled, multi-centre	Total=1284 NIMENRIX®=885 ACWY-PS=294 Co-admin=105	35.5 (18-55)	710/574
Men ACWY-TT -071	Immunogenicity and safety compared to quadrivalent meningococcal diphtheria toxoid conjugate vaccine (MENACTRA®)	Observer-blinded, randomized, controlled, multi-centre	Total =951 NIMENRIX®=637 MENACTRA®=314	16.3 (10-25)	464/487
> 55 years					
Men ACWY-TT-085	Immunogenicity, safety, and reactogenicity compared to ACWY-PS	Open, randomized, controlled	Total = 260 NIMENRIX®= 194 ACWY-PS= 66	63.9 (56-103)	178/82

[§]Number of subjects in according-to-protocol (ATP) cohort for immunogenicity or persistence

Study results

Immunogenicity in toddlers aged 12-23 months

In the clinical study MenACWY-TT-039, the immune response to vaccination with either NIMENRIX® or a licensed meningococcal C-CRM$_{197}$ conjugate (MenC-CRM) vaccine was evaluated.

NIMENRIX® elicited a bactericidal antibody response against the four serogroups, with a response against serogroup C that was comparable to the one elicited by the licensed MenC-CRM vaccine in term of rSBA titres ≥8 (Table 5)

Table 5 Study MenACWY-TT-039: Percentage of subjects with rSBA$^{\beta}$ titres equal to or above the cut off value of 1:8 at day 42 post vaccination

Serogroup	N	NIMENRIX® (95% CI)	N	Active Control (MenC-CRM)	Difference in percentage (ACWY-TT minus MenC-CRM)* (95%CI)
rSBA-Men A	354	99.7% (98.4; 100)	-	-	-
rSBA-Men C	354	99.7% (98.4; 100)	121	97.5% (92.9; 99.5)	2.20 (0.29; 6.78)
rSBA-MenW-135	354	100% (99.0; 100)	-	-	-
rSBA-Men Y	354	100% (99.0; 100)	-	-	-

N = number of subjects with results available
% = percentage of subjects with titre within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
ATP cohort for immunogenicity
*LL of 95% CI is above non-inferiority limit of -10%.
$^{\beta}$tested at GSK Laboratories

The Geometric Mean Titres (GMTs) for MenC 42 days after vaccination were higher in children who received NIMENRIX® than those who received MenC-CRM (478 vs. 212). GMTs ranged between 2205 and 2729 for serogroups A, W-135 and Y in the NIMENRIX® group.

In addition this study evaluated the immunogenicity for hSBA prior to and 42 days after the first vaccine dose with NIMENRIX® or the control vaccine (MenC-CRM). At 42 days after vaccination, 98.5% of the subjects in the NIMENRIX® group and 81.9% of subjects in the MenC-CRM group had hSBA-MenC titres ≥ 8. In the NIMENRIX® group the percentage of subjects with hSBA titres ≥ 8 ranged between 77.2% and 87.5 % for serogroups A, W-135 and Y.

Immunogenicity in children aged 2 to 10 years
In study (MenACWY-TT-081) conducted in subjects aged 2-10 years, one group of subjects received a dose of NIMENRIX® and a second group a dose of a licensed MenC-CRM vaccine as a comparator.

Table 6 Study MenACWY-TT-081: Percentage of subjects with a vaccine response in terms of rSBA* antibodies one month following vaccination

Serogroup	N	NIMENRIX® % (95% CI)	N	Active Control (MenC-CRM) % (95% CI)	Difference in vaccine response rate (ACWY-TT minus MenC-CRM) (95%CI)*
rSBA-Men A	226	94.7% (90.9; 97.2)	-	-	-
rSBA-Men C	268	94.8% (91.4; 97.1)	92	95.7% (89.2; 98.8)	-0.88 (**-5,25**; 5,57)
rSBA-MenW-135	282	98.6% (96.4; 99.6)	-	-	-
rSBA-Men Y	285	96.5% (93.6; 98.3)	-	-	-

Vaccine response defined as:
For initially seronegative subjects: post-vaccination antibody titre ≥ 1:32 at one month post-vaccination
For initially seropositive subjects: antibody titre at one month post-vaccination ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with pre- and post-vaccination results available
95% CI = Standardized asymptotic 95% confidence interval; LL = lower limit, UL = upper limit
Bold: LL of 95% CI is above non-inferiority limit of -10% for MenC.
*tested at GSK Laboratories

The non-inferiority of the NIMENRIX® vaccine compared to the MenC-CRM vaccine in terms of serum bactericidal antibody vaccine response to rSBA-MenC, one month after vaccination was demonstrated since the lower limit of the 95% CIs on the difference between the NIMENRIX® and (minus) the MenC-CRM group was -5.25%, which was above the pre-specified non-inferiority limit of -10%.

The GMT elicited by MenC-CRM was higher than the one observed for the NIMENRIX® vaccine (5291.6 vs. 2794.8). The percentage of subjects with rSBA-MenC titre ≥ 128 was similar for both vaccines (100% vs. 99.3%). For NIMENRIX® GMTs ranged between 6236.1 and 8549.5 for rSBA MenA, W-135 and Y.

Immunogenicity in adolescents aged 10-25 years and adults aged 18 up to 55 years
In a Phase II head-to-head study conducted in Canada and the US with NIMENRIX® and the licensed quadrivalent meningococcal diphtheria toxoid conjugate vaccine (ACWY-DT) MENACTRA® in subjects aged 10-25 years (study Men ACWY-TT-071), either one dose of NIMENRIX® or one dose of MENACTRA® was administered.

NIMENRIX® was demonstrated to be immunologically non-inferior to MENACTRA® in terms of the percentage of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY vaccine response one month after vaccination (all the lower limits of the two-sided 95% CI for the difference between groups were greater than or equal to -10%) (Table 7).

The GMT elicited by NIMENRIX® ranged from 49.6 to 755.8 for hSBA MenA, C, W-135 and Y and the GMT elicited by MENACTRA® ranged from 41.3 to 543.4 for hSBA MenA, C, W-135 and Y.

Table 7 Study Men ACWY-TT-071: Percentage of subjects with vaccine response to hSBA* antibodies one month following vaccination

Serogroup	N	NIMENRIX® % (95% CI)	N	(MENACTRA®) % (95% CI)	Difference in vaccine response rate (ACWY-TT Lot A minus ACWY-DT)* (95%CI)
hSBA-Men A	310	70.3% (64.9; 75.4)	297	64.3% (58.6; 69.8)	6.01 (**-1.45**: 13.44)
hSBA-Men C	281	77.2% (71.9; 82.0)	274	76.3% (70.8; 81.2)	0.95 (**-6.10**; 8.00)
hSBA-MenW-135	279	71.0% (65.3; 76.2)	289	64.0% (58.2; 69.6)	6.95 (**-0,76**; 14.59)
hSBA-Men Y	293	51.2% (45.3; 57.1)	295	39.0% (33.4; 44.8)	12.21 (**4,17**; 20.10)

Vaccine response defined as:
For initially seronegative subjects: post-vaccination antibody titer ≥ 1:8 at one month post-vaccination
For initially seropositive subjects: antibody titer at one month post-vaccination ≥ 4-fold the pre-vaccination antibody titer
N = number of subjects with pre- and post-vaccination results available
95% CI = Standardized asymptotic 95% confidence interval; LL = Lower Limit, UL = Upper Limit
Bold: LL of 95% CI is above non-inferiority limit of -10%.
*tested at GSK Laboratories

In another clinical study, conducted in adults 18-55 years of age (study MenACWY-TT-035), either one dose of NIMENRIX® or one dose of the ACWY-PS vaccine were administered.

Table 8 Study MenACWY-TT-035: Percentage of subjects with vaccine response to rSBA* antibodies one month following vaccination

Serogroup	N	NIMENRIX® % (95% CI)	N	Active Control (ACWY-PS) % (95% CI)	Difference in vaccine response rate (NIMENRIX® minus ACWY-PS) (95%CI)*
rSBA-Men A	743	80.1% (77.0; 82.9)	252	69.8% (63.8; 75.4)	10.24 (**4.11**; 16.78)
rSBA-Men C	849	91.5% (89.4; 93.3)	288	92.0% (88.3; 94.9)	-0.49 (**-3.85**; 3.57)
rSBA-MenW-135	860	90.2% (88.1; 92.1)	283	85.5% (80.9; 89.4)	4.72) (**0.49**; 9.65)
rSBA-Men Y	862	87.0% (84.6; 89.2)	288	78.8% (73.6; 83.4)	8.19 (**3.24**; 13.69)

Vaccine response defined as:
For initially seronegative subjects: post-vaccination antibody titre ≥ 1:32 at one month post-vaccination
For initially seropositive subjects: antibody titre at one month post-vaccination ≥ 4 fold the pre-vaccination antibody titre
N = number of subjects with pre- and post-vaccination results available
95% CI = Standardized asymptotic 95% confidence interval; LL = lower limit, UL = upper limit
Bold: LL of 95% CI is above non-inferiority limit of -10%
*tested at GSK Laboratories

The response to the four meningococcal groups elicited by NIMENRIX® was either similar or higher than the one elicited by the ACWY-PS vaccine. In adults, NIMENRIX® was demonstrated to be immunologically non-inferior to the ACWY-PS vaccine. NIMENRIX®

induced higher GMTs and vaccine response for serogroups A, W-135 and Y than the ACWY-PS vaccine.

The GMT elicited by NIMENRIX® ranged from 3624.7 to 8865.9 for rSBA MenA, C, W-135 and Y and the GMT elicited by MENACTRA® ranged from 2127.2 to 7371.2 for rSBA MenA, C, W-135 and Y.

Immunogenicity in adults aged > 55 years
A descriptive study (MenACWY-TT-085) was conducted to evaluate the immunogenicity of NIMENRIX® compared to ACWY-PS vaccine, in terms of Meningococcal serogroups A, C, W-135 and Y bactericidal vaccine response[a] one month after the vaccination. A single dose of vaccine was administered to 369 Lebanese adults 56 years of age and older (including 274 and 95 subjects in the treatment and control groups, respectively). The analysis of immunogenicity was evaluated based on 260 subjects included in the ATP cohort for immunogenicity (194 and 66 subjects in the treatment and control groups, respectively). The vaccine response ranged from 76.6% (rSBA-MenA) to 81.9% (rSBA-MenY) in the NIMENRIX® group and from 84.8% (rSBA-MenC) to 91.7% (rSBA-MenA) in the ACWY-PS group. Of the 194 subjects in the treatment group, the percentage of subjects with rSBA titres ≥ 128 before vaccination ranged from 45% (MenC) to 62% (MenY). Overall, at one month post-vaccination the percentage of vaccinees with rSBA titres ≥ 128 ranged from 93% (MenC) to 97% (MenY). The supplementary analysis showed that in the subgroup aged > 65 years the percentage of vaccinees with rSBA titres ≥ 128 at one month post-vaccination ranged from 90% (MenA) to 97% (MenY).

Persistence of immune response
The persistence of the immune response elicited by NIMENRIX® was evaluated up to 60 months after vaccination in subjects aged 12 months to 55 years.

For all serogroups (A, C, W-135, Y), the persistence of the antibodies elicited by NIMENRIX® was similar or higher than those induced by the licensed meningococcal vaccines [i.e. MenC-CRM vaccine in subjects aged 12-23 months, and ACWY-PS vaccine in subjects older than 2 years of age, and MENACTRA® in subjects aged 11-25 years].

Persistence of immune response in toddlers aged 12-23 months
In study MenACWY-TT-048, the persistence of the immune response was evaluated by rSBA and hSBA up to four years in toddlers in terms of percentage of subjects with antibody titres ≥ 1:8 for each of the 4 serogroups in toddlers primed in study MenACWY TT 039.

Forty-eight months following primary vaccination, 27% of the children were included in this evaluation (Table 9).

[a]Vaccine response to meningococcal antigens (MenA, MenC, MenW-135 and MenY) at one month post vaccination, defined as:
- for initially seronegative subjects (rSBA titre less than 1:8), post vaccination rSBA titre ≥ 1:32
- for initially seropositive subjects with rSBA titre between 1:8 and 1:128, at least four-fold increase in rSBA titre from pre to post vaccination
- for initially seropositive subjects with rSBA titres ≥ 1:128, at least two-fold increase in rSBA titre from pre to post vaccination

Table 9 4 years persistence data in toddlers aged 12-23 months at vaccination (study MenACWY-TT-048)

Serogroup	Group	Time-point (Year)	rSBA*		hSBA**	
			N	% Response	N	% Response
A	**NIMENRIX®**	3	262	59.9%	251	35.9%
		4	224	74.1%	198	28.8%
C	**NIMENRIX®**	3	262	35.9%	253	78.3%
		4	225	40.4%	209	73.2%
	MenC-CRM vaccine	3	46	13.0%	31	41.9%
		4	45	35.6%	32	46.9%
W-135	**NIMENRIX®**	3	261	49.8%	254	82.3%
		4	225	49.3%	165	80.6%
Y	**NIMENRIX®**	3	262	53.8%	250	72.0%
		4	225	58.2%	130	65.4%

The analysis of immunogenicity was conducted on ATP cohort for persistence adapted for each time-point.
*rSBA testing performed at Public Health England (PHE) laboratories in UK
** tested at GSK laboratories
Vaccine response defined as: post-vaccination antibody titre ≥ 1:8

In study MenACWY-TT-032, the persistence of the immune response was evaluated by rSBA and hSBA in toddlers aged 12-23 months up to 5 years. At year 5, for all four serogroups W-135, Y, A and C, 34.7%, 42.9%, 73.5% and 77.6% of subjects in the NIMENRIX® group had rSBA titres ≥ 1:8, respectively. In the MenC-CRM group, 63.6% of subjects had rSBA MenC titres ≥ 1:8 for serogroup C. For serogroups C, W-135 and Y, at least 80.0% of subjects in the NIMENRIX® group had hSBA titres ≥ 1:8; for serogroup A this was only 35.6%. In the MenC-CRM group, 90.9% of subjects had hSBA-MenC titres ≥ 1:8.

Persistence of immune response in children aged 2-10 years
In study MenACWY-TT-088 (Table 10), the persistence of the immune response was evaluated by rSBA and hSBA up to 44 months after vaccination in children 2-10 years of age primed in study MenACWY-TT-081 (Table 6).

Table 10 44 months persistence data in children aged 2-10 years at vaccination (study MenACWY-TT-088)

Serogroup	Group	Time-point (months)	rSBA*		hSBA**	
			N	% response	N	% response
A	**Nimenrix**	32	193	86.5%	90	25.6%
		44	189	85.7%	89	25.8%
C	**Nimenrix**	32	192	64.6%	90	95.6%
		44	189	37.0%	82	76.8%
	MenC-CRM vaccine	32	69	76.8%	33	90.9%
		44	66	45.5%	31	64.5%
W-135	**Nimenrix**	32	193	77.2%	86	84.9%
		44	189	68.3%	87	80.5%
Y	**Nimenrix**	32	193	81.3%	91	81.3%
		44	189	62.4%	76	82.9%

The analysis of immunogenicity was conducted on ATP cohort for persistence adapted for each time-point.
*rSBA testing performed at PHE laboratories in UK
** tested at GSK laboratories
Vaccine response defined as: post-vaccination antibody titre ≥ 1:8

Persistence of immune response vs. MENACTRA® in adolescents and adults aged 11-25 years evaluated by hSBA

In study MenACWY-TT-059, the persistence of the immune response was evaluated by hSBA 1 and 3 years after vaccination compared to MENACTRA® in adolescents and adults 11-25 years of age primed in study MenACWY-TT-052 (Table 11). At 1 and 3 years following the primary vaccination 64% and 58% of the subjects were included in the evaluation, respectively.

For all groups (A, C, W-135, Y), the persistence of the antibodies elicited by NIMENRIX® was similar or higher than those induced by MENACTRA®.

Table 11 1 month post-vaccination and 3 years persistence data in adolescents and adults 11-25 years of age evaluated by hSBA*

Serogroup	Time-point	N	NIMENRIX® %	N	Active Control (MENACTRA®) %
hSBA-Men A	Month 1	356	82.0%	108	73.1%
	Year 1	350	29.1%	112	31.3%
	Year 3	316	37.3%	79	48.1%
hSBA-Men C	Month 1	359	96.1%	114	99.1%
	Year 1	336	94.9%	105	73.3%
	Year 3	319	93.1%	81	81.5%
hSBA-MenW-135	Month 1	334	91.0%	97	75.3%
	Year 1	327	98.5%	108	75.9%
	Year 3	323	95.4%	80	85.0%
hSBA-Men Y	Month 1	364	95.1%	112	81.3%
	Year 1	356	97.8%	113	86.7%
	Year 3	321	96.0%	80	88.8%

The analysis of immunogenicity was conducted on ATP cohort for persistence adapted for each time-point.
* tested at GSK laboratories

Vaccine response defined as: post-vaccination antibody titre ≥ 1:8

Immune memory

In study MenACWY-TT-014, the induction of immune memory was assessed one month after the administration of a fifth of the dose of ACWY-PS vaccine (10 µg of each polysaccharide) to children in the third year of life previously primed in the study MenACWY-TT-013 with NIMENRIX® or a licensed MenC-CRM vaccine at the age of 12 to 14 months.

One month after the challenge dose, the GMTs elicited by the subjects primed with NIMENRIX® increased by 6.1 to 34 fold for serogroups A, C, W-135 and Y and indicate that NIMENRIX® induces immune memory to serogroups A, W-135 and Y. The post-challenge rSBA-MenC GMT was similar in both study groups, indicating that NIMENRIX® induces an analogous immune memory to serogroup C as the licensed MenC-CRM vaccine (Table 12).

Table 12 Immune response (rSBA*) 1 month after a challenge vaccination in subjects primed with NIMENRIX® or a MenC-CRM vaccine at the age of 12 to 14 months

Group	Response to	Pre-challenge		Post-challenge	
		N	GMT	N	GMT
A	NIMENRIX®	32	544	25	3322
C	NIMENRIX®	31	174	32	5966
	MenC-CRM vaccine	28	34	30	5265
W-135	NIMENRIX®	32	644	32	11058
Y	NIMENRIX®	32	440	32	5737

The analysis of immunogenicity was conducted on ATP cohort for immunogenicity.
*tested at GSK Laboratories

Booster response
In study MenACWY-TT-048, a booster response was evaluated in children vaccinated 4 years earlier (at toddler age) in study MenACWY-TT-039 (Table 13). Children were primed and boosted with the same vaccine: either NIMENRIX® or a MenC-CRM vaccine. A robust increase in rSBA and hSBA GMTs was observed from pre booster dose to one month post booster dose of NIMENRIX® (Table 13).

Table 13 Immune response (rSBA* and hSBA) pre-booster and 1 month after post-booster in subjects vaccinated either with NIMENRIX® or a MenC-CRM vaccine 4 years earlier (at toddler age)**

Group	Response to	Time Point	rSBA*		hSBA**	
			N	GMT	N	GMT
A	NIMENRIX®	Pre-Booster	212	112	187	5
		Post-Booster	214	7173	202	1343
C	NIMENRIX®	Pre-Booster	213	12	200	31
		Post-Booster	215	4512	209	15831
	MenC-CRM vaccine	Pre-Booster	43	14	31	12
		Post-Booster	43	3718	33	8646
W-135	NIMENRIX®	Pre-Booster	213	30	158	48
		Post-Booster	215	10950	192	14411
Y	NIMENRIX®	Pre-Booster	213	37	123	30
		Post-Booster	215	4585	173	6776

The analysis of immunogenicity was conducted on the booster ATP cohort for immunogenicity.
*rSBA testing performed at HPA laboratories in UK
**tested at GSK laboratories

Subjects previously vaccinated with a plain polysaccharide vaccine against *Neisseria meningitides*
In study MenACWY-TT-021 conducted in subjects aged 4.5-34 years, the immunogenicity of NIMENRIX® administered between 30 and 42 months after vaccination with a ACWY-PS vaccine was compared to the immunogenicity of NIMENRIX® administered to age-matched

subjects who had not been vaccinated with any meningococcal vaccine in the preceding 10 years. An immune response (rSBA titre ≥8) was observed against all serogroups (A, C, W-135, Y) in all subjects regardless of the meningococcal vaccine history. The rSBA GMTs were significantly lower in the subjects who had received a dose of ACWY-PS vaccine 30-42 months prior to NIMENRIX®. However, rSBA GMTs did increase post-vaccination for all four serogroups, ranging from 3.9- to 30.1- fold in the ACWY-PS group and from 11.8- to 246.0-fold in the no ACWY-PS group. At least 97.0% of the subjects in the ACWY-PS group demonstrated post-vaccination rSBA titres ≥ 1:128 for all four serogroups.

TOXICOLOGY

Non-clinical data reveal no special hazard for humans based on local tolerance, acute toxicity, repeated dose toxicity, developmental/reproductive toxicity and fertility studies.

Table 14 Nonclinical toxicology studies

Study type and species	Route and dosage regimen	Results
Local tolerance and acute toxicity New Zealand White rabbit	One intramuscular injection; full human dose	No distinct treatment-related changes in general and local clinical signs and body weight. No macroscopic abnormalities seen at injection site. A slight mononuclear type inflammation was observed microscopically at the injection sites of both the saline control and MenACWY-TT groups.
Repeated dose toxicity New Zealand White rabbit	Five repeated intramuscular injections two weeks apart; full human dose per injection	No treatment-related changes observed in general and in local clinical signs, ophthalmoscopy, rectal body temperature, haematology, clinical chemistry or organ weights. Very slight to slight inflammation in the injected muscles which diminished distinctly over time with a clear recovery process observed 28-days after the last dose. No adverse vaccine formulation-related histopathological changes were observed any other tissues or organs.
Reproductive and developmental toxicity Wistar rat	Intramuscular injection 42 and 28 days before mating and on gestation days 6, 8, 11 and 15; 2/5 of the full human dose per injection (200 µl)	No treatment-related effects on maternal toxicity, prenatal development (including external, visceral and skeletal abnormalities), or postnatal development

REFERENCES

1. Baxter, R., Baine, Y., Ensor, K., Bianco, V, Friedland, L, Miller, J. (2011). Immunogenicity and Safety of an Investigational Quadrivalent Meningococcal ACWY Tetanus Toxoid Conjugate Vaccine in Healthy Adolescents and Young Adults 10 to 25 Years of Age. Pediatric Infectious Disease Journal; 30(3): e41-48.

2. Bermal, N., Huang, L., Dubey, A.P., Jain, H, Bavdekar, A, et al. (2011). Safety and immunogenicity of a tetravalent meningococcal serogroups A, C, W-135 and Y conjugate vaccine in adolescents and adults. (2011). Human Vaccines; 7(2): 239-247.

3. Bettinger, J. A., Scheifele, D. W., Le Saux, N., Halperin, S, Vaudry, W, et al. (2009). The Impact of Childhood Meningococcal Serogroup C Conjugate Vaccine Programs in Canada. The Pediatric Infectious Disease Journal; 28(3): 220-224.

4. Knuf, M., Kieninger-Baum, D, Habermehi, P, Muttonen, P, Maurer, H, Vink, Pl. (2010). A dose-range study assessing immunogenicity and safety of one dose of a new candidate meningococcal serogroups A, C, W-135, Y tetanus toxoid conjugate (MenACWY-TT) vaccine administered in the second year of life and in young children.. Vaccine; 28: 744-753.

5. Knuf, M., Pantazi-Chatzikonstantinou, A., Pfletschinger, U., Tichmann-Schumann, I, Maurer, H, et al. (2011). An investigational tetravalent meningococcal serogroups A, C, W-135 and Y-tetanus toxoid conjugate vaccine co-administered with Infanrix^{TM} hexa is immunogenic, with an acceptable safety profile in 12–23-month-old children. Vaccine; 29: 4264-4273.

6. Law, D., Lorange, M, Ringuette, L, Dion, R, Giguere, M, et al. (2006). Invasive Meningococcal Disease in Quebec, Canada, Dur to an Emerging Clone of ST-269 Serogroup B Meningococci with Serotype Antigen 17 and Serosubtype Antigen P1.19 (B:17:P1.19).

7. Le Saux, N., Bettinger, J.A., Wootton, S., et al. (2009). Profile of serogroup Y meningococcal infections in Canada: Implications for vaccine selection. Canadian Journal of Infectious Diseases, Medical Microbiology; 20(4): e130-134.

8. Memish, Z.A., Dbaibo, G., Montellano, M., Verghese, V, Jain, H, et al. (2011). Immunogenicity of a Single Dose of Tetravalent Meningococcal Serogroups A, C, W-135, and Y Conjugate Vaccine Administered to 2- to 10-year-olds Is Noninferior to a Licensed- ACWY Polysaccharide Vaccine With an Acceptable Safety Profile. The Pediatric Infectious Disease Journal; 30 (4): e56-62.

9. Ostergaard, L, Lebacq, E, Poolman, Maechler, G, Boutriau, D. (2009). Immunogenicity, reactogenicity and persistence of meningococcal A, C, W-135 and Y-tetanus toxoid candidate conjugate (MenACWY-TT) vaccine formulations in adolescents aged 15-25 years. Vaccine, 27:161-168.

10. Ostergaard, L, Silfverdal, SA, Berglund, J, Flodmark, C-E, West, C, et al. (2012). A tetravalent meningococcal serogroups A, C, W-135 and Y tetanus toxoid conjugate vaccine is immunogenic and well-tolerated when co-administered with Twinrix® in subjects aged 11-17 years: An open, randomized, controlled trial.. Vaccine, 30:774-783.

11. Public Health Agency of Canada. An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI). Update on the invasive meningococcal disease and meningococcal vaccine conjugate recommendations. Canada Communicable Disease Report. April 2009; Volume 36, ACS-3:1-40.

12. Public Health Agency of Canada. An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI). Statement on conjugate menincococcal vaccine for serogroups A, C, Y and W-135. Canada Communicable Disease Report 2007; 33.

13. Public Health Agency of Canada, Meningococcal Disease. 2001. Accessed on Aug 25, 2011. Accessed from: http://www.phac-aspc.gc.ca/publicat/info/infmen-eng.php

14. Public Health Agency of Canada. Enhanced surveillance of invasive meningococcal disease in Canada: 1 January, 2002-31 December 2003. - April, 2006. Accessed on August 25, 2011 Accessed from: http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/06vol32/dr3208a-eng.php

15. Public Health Agency of Canada. Invasive Meningococcal Disease (IMD) http://www.phac-aspc.gc.ca/im/vpd-mev/meningococcal-eng.php

16. Vesikari, T., Karvonen, A., Bianco, V., VanderWielen, M, Miller, J. (2011). Tetravalent meningococcal serogroups A, C, W-135 and Y conjugate vaccine is well tolerated and immunogenic when co-administered with measles–mumps–rubella–varicella vaccine during the second year of life: An open, randomized controlled trial. Vaccine; 29: 4274-4284.

PART III: CONSUMER INFORMATION

NIMENRIX®
Meningococcal polysaccharide groups A, C, W-135 and Y conjugate vaccine

This leaflet is part III of a three-part "Product Monograph" published when NIMENRIX® was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about NIMENRIX®. Contact your health professional if you have any questions about the vaccine.

ABOUT THIS VACCINE

What the vaccine is used for:
NIMENRIX® is a vaccine that may be given to persons 12 months to 55 years old to prevent illness caused by *Neisseria meningitidis* types A, C, W-135 and Y bacteria (germs).

Neisseria meningitidis types A, C, W-135 and Y bacteria most often cause meningitis (infection of the tissue lining the brain) and septicemia (infection of the blood). These diseases can be highly infectious and are sometimes fatal.

As with all vaccines, NIMENRIX® may not fully protect all people who are vaccinated.

NIMENRIX® will only protect against infections caused by groups of *Neisseria meningitidis* for which the vaccine has been developed.

What it does:
The vaccine works by causing the body to produce its own protection (antibodies) against these bacteria. The vaccine cannot cause these diseases.

When it should not be used:
Please see WARNINGS AND PRECAUTIONS section.

What the medicinal ingredient is:
Each 0.5 mL dose contains 5 micrograms of each of the *Neisseria meningitidis* capsular polysaccharides A, C, W-135 and Y each coupled to tetanus toxoid as a carrier protein.

What the important non-medicinal ingredients are:
NIMENRIX® contains the following non-medicinal ingredients:

- Powder: sucrose, trometamol
- Diluent: sodium chloride, water for injections

What dosage forms it comes in:
NIMENRIX® is presented as a powder and diluent for solution for injection.

WARNINGS AND PRECAUTIONS

NIMENRIX® should not be given if you have previously had any allergic reaction to NIMENRIX®, or any ingredient contained in NIMENRIX®. Signs of an allergic reaction may include itchy skin rash, shortness of breath and swelling of the face or tongue.

BEFORE you use NIMENRIX® talk to your health professional if:

- you or your child have/has a severe infection with a high temperature. In these cases, the vaccination will be postponed until recovery. A minor infection such as a cold should not be a problem, but talk to your health professional first.
- you or your child have/has a bleeding problem or bruise(s) easily.
- you or your child have/has a weakened immune system, for example due to HIV infection or due to medicines that suppress the immune system. You or your child may not get the full benefit from NIMENRIX®.
- you are pregnant or breastfeeding.

Fainting can occur following, or even before, any needle injection, therefore tell your health professional if you/your child fainted with a previous injection.

INTERACTIONS WITH THIS VACCINE

Please tell your health professional if you/your child are/is taking or have/has recently taken any other medicines, including medicines obtained without a prescription or have/has recently received any other vaccine.

NIMENRIX® may not work as well if you/your child are/is taking medicines that reduce the effectiveness of your/your child's immune system to fight infection.

NIMENRIX® can be given at the same time as other vaccines such as hepatitis A and hepatitis B vaccines, measles-mumps-rubella vaccine, measles-mumps-rubella-varicella vaccine, 10-valent pneumococcal conjugate vaccine or unadjuvanted seasonal influenza vaccine.

In the second year of life, NIMENRIX® can also be given at the same time or at least one month before a combined diphtheria - tetanus - acellular pertussis vaccines, including combination diphtheria - tetanus - acellular pertussis vaccines with hepatitis B, inactivated polio or *Haemophilus influenzae* type b, such as DTPa-HBV-IPV/Hib vaccine.

A different injection site will be used for each vaccine.

PROPER USE OF THIS VACCINE

Usual dose:
Your health professional will give NIMENRIX® as an injection into the muscle. NIMENRIX® is given as one injection of 0.5 mL.

Overdose:

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

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

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

In infants, adolescents and adults, very common side effects (in more than 1 in 10 doses of the vaccine) after having NIMENRIX® are loss of appetite, irritability, drowsiness, headache, fever, swelling, pain and redness at the injection site and fatigue.

Common side effects (in more than 1 in 100 doses of the vaccine) after having NIMENRIX® are gastrointestinal symptoms including diarrhoea, vomiting and nausea, and injection site hematoma.

Uncommon side effects (in more than 1 in 1,000 doses of the vaccine) after having NIMENRIX® are insomnia, crying, dizziness, decreased feeling or sensitivity especially in the skin, itching, rash, aching muscles, pain in extremity (pain in the limb), generally feeling unwell, and injection site reaction (such as a hard lump at the injection site, itching warmth and loss of feeling).

The most common side effects reported during clinical trials usually lasted only one to two days and were not usually severe.

The following additional side effect has been reported rarely (in up to 1 in 1,000 doses of the vaccine): large swelling of the vaccinated limb associated with redness.

Tell your health professional as soon as possible if you or your child does not feel well after receiving NIMENRIX®.

Do not be alarmed by this list of possible side effects. It is possible that you or your child will have no side effects from vaccination.

This is not a complete list of side effects. For any unexpected effects while taking NIMENRIX®, contact your health professional.

HOW TO STORE IT

Keep out of reach and sight of children. Store in a refrigerator (2°C – 8°C). Do not freeze. Store in the original package in order to protect from light.

REPORTING SUSPECTED SIDE EFFECTS

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

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

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

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

By toll-free telephone: 1-866-844-0018
By toll-free fax: 1-866-844-5931
By email: caefi@phac-aspc.gc.ca
At the following website:
http://www.phac-aspc.gc.ca/im/vs-sv/index-eng.php

By regular mail:
The Public Health Agency of Canada
Vaccine Safety Section
130 Colonnade Road
Ottawa, Ontario
K1A 0K9 Address Locator 6502A

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

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at www.pfizer.ca or by contacting the sponsor,
Pfizer Canada Inc.
at: 1-800-463-6001 (Medical Information)

This leaflet was prepared by Pfizer Canada Inc.

Last revised: March 23, 2016