PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

NeisVac-C® Vaccine

Meningococcal Group C-TT Conjugate Vaccine, Adsorbed Suspension for Injection

10 mcg *Neisseria meningitidis* group C polysaccharide suspension for intramuscular injection

Active Immunizing Agent

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

Date of Initial Authorization:
December 18, 2001

Date of Revision:
October 26, 2021

Submission Control Number: 253221

RECENT MAJOR LABEL CHANGES

Warnings and Precautions	05/2019

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Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

NeisVac-C® vaccine (meningococcal group C-TT conjugate vaccine, adsorbed) is indicated for:

- Active immunization of children from 2 months of age, adolescents and adults, for the prevention of meningitis and/or septicemia caused by *Neisseria meningitidis* serogroup C.

1.1 Pediatrics

Pediatrics (2 months of age and older): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of NeisVac-C® vaccine in pediatric patients has been established. Therefore, Health Canada has authorized an indication for pediatric use.

1.2 Geriatrics

Geriatrics (adults 65 years or older): Although the vaccine has been studied in adults, studies have not been conducted in adults 65 years or older.

2 CONTRAINDICATIONS

- Known or suspected hypersensitivity to NeisVac-C® vaccine (meningococcal group C-TT conjugate vaccine, adsorbed), or to any of its components including tetanus toxoid (see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING).

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

Serious Warnings and Precautions
• **NeisVac-C® vaccine should under no circumstances be injected intravenously or subcutaneously.**

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

There are no data on the use of different meningococcal group C conjugate vaccines within the primary series or for boosting. Whenever possible, the same vaccine should be used throughout.

4.2 Recommended Dose and Dosage Adjustment

Primary Immunization:

Infants from 2 months of age up to 4 months: Two doses, each of 0.5 mL, should be given with an interval of at least two months. The second dose should be administered when the infant is older than five months of age (see 14 CLINICAL TRIALS).

Infants from 4 months of age, older children, adolescents and adults: One dose of 0.5 mL.

Booster Doses:

After completion of the primary immunization course in infants aged 2 months up to 12 months of age, a booster dose should be given at approximately 12 to 13 months of age, with an interval of at least 6 months after the last NeisVac-C® vaccination.

In subjects aged 12 months or more when first immunized, the necessity of a booster dose has not been established, (see 14 CLINICAL TRIALS).

4.4 Administration

The vaccine must not be administered subcutaneously or intravenously (See 7 WARNINGS AND PRECAUTIONS section)**.**

NeisVac-C® vaccine must not be mixed with other vaccines in the same syringe. Separate injection sites should be used if more than one vaccine is being administered on the same day.

NeisVac-C® vaccine is for intramuscular injection, preferably in the anterolateral thigh region in infants and the deltoid region in older children, adolescents and adults.

In children 12 to 24 months of age, the vaccine may be administered in the deltoid or the anterolateral thigh.

Upon storage, a white deposit and clear supernatant can be observed. The vaccine should be well shaken in order to obtain a homogenous suspension and inspected for foreign particulate matter and discoloration prior to administration. Do not administer if particulate matter or discoloration is found.

4.5 Missed Dose

Missing a dose is highly unlikely, since it is administered as a single dose by a health care provider.

4.6 Instructions for Preparation and Use

- Shake well prior to administration to thoroughly mix the vaccine suspension.
- After shaking, the vaccine should be a homogeneous semi-opaque white to off-white suspension.
- The vaccine should be inspected visually for any foreign particulate matter and/or variation in physical appearance prior to administration whenever solution and container permit. In the event of either being observed, discard the vaccine.

5 OVERDOSAGE

Overdosing with the vaccine is highly unlikely, since it is administered from a single dose syringe by a health care provider.

In a published clinical study in infants, 40 subjects received three doses of NeisVac-C® at 2, 3, and 4 months and a fourth dose at 12-14 months of age. All four vaccine doses were well tolerated with no serious vaccine related adverse events.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 1 – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Intramuscular	• *Neisseria meningitidis* group C polysaccharide conjugated • tetanus toxoid protein	Aluminium hydroxide, Sodium chloride and water for injection

NeisVac-C® vaccine (meningococcal group C-TT conjugate vaccine, adsorbed) is a semi-opaque white to off-white suspension. It is presented as a 0.5 mL suspension in a pre-filled syringe with a rubber cap and a rubber plunger stopper.

Description

One dose of 0.5 mL NeisVac-C® vaccine contains:

Neisseria meningitidis group C polysaccharide	10 mcg
tetanus toxoid	10-20 mcg
aluminum hydroxide	0.5 mg Al3+
sodium chloride	4.1 mg

Packaging

NeisVac-C® vaccine is available in packs of 1, 10 or 20 syringes

7 WARNINGS AND PRECAUTIONS

General

NeisVac-C® vaccine (meningococcal group C-TT conjugate vaccine, adsorbed) will only confer protection against group C of *Neisseria meningitidis* and may not completely prevent meningococcal group C disease. It will not protect against other groups of *Neisseria meningitidis* or other organisms that cause meningitis or septicaemia.

Adequate medical treatment and provisions should be available for immediate use in the rare event of an anaphylactic reaction. For this reason the subject should remain under supervision for the appropriate length of time after vaccination.

As with any vaccine, administration of NeisVac-C® vaccine should be postponed for subjects suffering from acute severe febrile illness.

This vaccine does not replace routine tetanus immunization.

No data on the applicability of the vaccine in outbreak control are yet available.

There is no evidence that the vaccine causes meningococcal C meningitis. Clinical alertness to the possibility of coincidental meningitis should therefore be maintained.

In the event of petechiae and/or purpura following vaccination, the aetiology should be thoroughly investigated. Both infective and non-infective causes should be considered.

Hematologic

To avoid the possibility of excessive bleeding, the vaccine should be given with caution to individuals with thrombocytopenia or any coagulation disorder.

Immune

In subjects deficient in producing antibody (e.g., due to genetic defect, HIV infection or immunosuppressive therapy) this vaccine may not induce protective antibody levels following vaccination. Hence, vaccination may not result in an appropriate protective antibody response in all individuals.

It would be anticipated that functionally or anatomically asplenic individuals would mount an immune response to meningococcal C conjugate vaccines; however, there are no specific data available regarding immune responses in these patient groups.

Individuals with certain complement deficiencies and individuals receiving treatment that inhibits terminal complement activation (for example, eculizumab) are at increased risk for invasive disease caused by *Neisseria meningitidis* serogroup C even if they develop antibodies following vaccination with NeisVac-C®.

Non-conjugated meningococcal polysaccharide vaccines should not be used for booster vaccination as they may negatively influence the immunologic memory.

Reproductive Health: Female and Male Potential

- **Fertility**

  The effects of NEISVAC-C on fertility have not been established in clinical trials. Animal studies do not indicate direct or indirect harmful effects with respect to fertility in females or males. Because animal reproductive studies are not always predictive of the human response, this vaccine should be used during pregnancy only if clearly needed.

Respiratory

The potential risk of apnea and the need for respiratory monitoring for 48-72 hours should be considered when administering the primary immunization series to very premature infants (born ≤28 weeks of gestation) and particularly for those with a previous history of respiratory immaturity.

As the benefit of vaccination is high in this group of infants, vaccination should not be withheld or delayed.

7.1 Special Populations

7.1.1 Pregnant Women

The safety of the vaccine during pregnancy and lactation has not been established. The vaccine should not be used during pregnancy unless there is a defined risk of meningococcal C disease, in which case the risk/benefit relationship should be evaluated. The risk/benefit relationship should also be examined before making the decision as to whether to immunize during lactation.

7.1.2 Breast-feeding

It is unknown if NeisVac-C® vaccine is excreted in human milk. The risk/benefit relationship should be examined before making the decision as to whether to immunize during lactation.

7.1.3 Pediatrics

Pediatrics (2 months of age and older): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of NeisVac-C® vaccine in pediatric patients has been established. Therefore, Health Canada has authorized an indication for pediatric use.

7.1.4 Geriatrics

Although the vaccine has been studied in adults, studies have not been conducted in adults 65 years or older.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

Although very rare, anaphylaxis and serious hypersensitivity reactions have occurred with all injectable vaccines, including NeisVac-C® vaccine (meningococcal group C-TT conjugate vaccine, adsorbed). When signs or symptoms of anaphylaxis or hypersensitivity occur (bronchospasm, facial oedema, angioedema, rash, hypotension or faints), they usually develop very quickly after the injection is given and while the person affected is still in the clinic or doctor's office.

The most common adverse reactions that have been reported are injection site reactions (redness, tenderness/pain, swelling), headache and fever, drowsiness and somnolence, or impaired sleeping, myalgia in the arms or legs (in all age groups); decreased appetite, vomiting, nausea or diarrhea, crying and irritability (in infants and/or toddlers); decreased appetite, vomiting, nausea or diarrhea (in older children).

In rare cases, in patients with pre-existing nephrotic syndrome, reoccurrence has been reported to present within a few months following vaccination with meningococcal group C polysaccharide conjugated vaccines. Signs of reoccurrence include angioedema, proteinuria and/or abnormal weight gain.

In addition, although very rare, other adverse reactions have been reported following product availability (see Post-Market Adverse Drug Reactions).

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials, therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

In controlled clinical studies performed in all age groups, signs and symptoms were actively monitored and recorded on diary cards following administration of the vaccine. Of the local solicited symptoms, the most frequently reported were injection-site pain, erythema and swelling. Fevers may also occur following vaccination, but these are rarely severe.

The most common adverse reactions reported in clinical studies in adults are presented in the following table.

Table 2 - Clinical Trial Adverse Reactions for Adults (>18 years of age) (N=130)

System Organ Class	ADR Term	Frequency (%)
Blood and lymphatic system disorders	Lymphadenopathy	1 (0.77%)
Gastrointestinal disorders	Vomiting	2 (1.54%)
General disorders and administration site conditions	Injection site tenderness/pain	109 (83.85%)
	Injection site erythema	40 (30.77%)
	Injection site swelling	26 (20.00%)
	Malaise	6 (4.62%)
	Fever	3 (2.31%)
	Influenza-like illness	1 (0.77%)
Musculoskeletal and connective tissue disorders	Myalgia	2 (1.54%)

Table 2 - Clinical Trial Adverse Reactions for Adults (>18 years of age) (N=130)		
System Organ Class	**ADR Term**	**Frequency (%)**
Nervous system disorders	Headache	16 (12.31%)

8.2.1 Clinical Trial Adverse Reactions – Pediatrics

The general symptoms that have been solicited and reported included irritability, somnolence, change in appetite, diarrhea, and fever in infants and younger children. These solicited general symptoms were also reported in the control groups and have been reported when NeisVac-C® vaccine was administered concomitantly with other vaccines.

In infants and toddlers, symptoms including crying, irritability, drowsiness, impaired sleeping, decreased appetite, diarrhea and vomiting were common after vaccination but there was no evidence that these were related to NeisVac-C® vaccine rather than concomitant vaccines, particularly DTP.

Commonly reported adverse events include headache (ranging from 1 in 7 secondary school children to 1 in 20 primary school children) and irritability (ranging from 1 in 2 babies to 1 in 25 pre-school children) and somnolence in younger children.

Table 3 - Clinical Trial Adverse Reactions for Infants (≤12 months of age) and Toddlers (12 months to 17 months of age) (N=2211)[1]		
System Organ Class	**ADR Term**	**Frequency (%)**
Infections and infestations	Pharyngitis/Rhinitis	35 (1.58%)
Immune system disorders	Hypersensitivity reaction (incl. bronchospasm)	1 (0.05%)
Metabolism and nutrition disorders	Decreased appetite	683 (30.89%)
Psychiatric disorders	Sleep disorder (impaired sleeping)	238 (10.76%)
	Agitation/Restlessness	40 (1.81%)
Nervous system disorders	Sedation/Somnolence/Fatigue[2]	807 (36.50%)
	Crying	628 (28.40%)
Eye disorders	Eyelid oedema	1 (0.05%)
Vascular disorders	Flushing	2 (0.09%)
	Circulatory collapse	1 (0.05%)
Respiratory, thoracic and mediastinal disorders	Cough	17 (0.77%)
Gastrointestinal disorders	Vomiting	322 (14.56%)
	Diarrhoea	85 (3.84%)
	Dyspepsia	11 (0.50%)
	Abdominal pain	8 (0.36%)
Skin and subcutaneous tissue disorders	Hyperhidrosis	76 (3.44%)
	Rash	33 (1.49%)
	Erythema	4 (0.18%)
	Dermatitis	2 (0.09%)
	Ecchymosis	1 (0.05%)
Musculoskeletal and connective tissue disorders	Pain in extremity	3 (0.14%)
	Musculoskeletal stiffness (incl. neck stiffness, joint stiffness)	1 (0.05%)
General disorders and administration site conditions	Irritability	1174 (53.10%)
	Fever	654 (29.58%)

Table 3 - Clinical Trial Adverse Reactions for Infants (≤12 months of age) and Toddlers (12 months to 17 months of age) (N=2211)[1]

System Organ Class	ADR Term	Frequency (%)
	Injection site erythema	602 (27.23%)
	Injection site tenderness/pain	416 (18.82%)
	Injection site swelling	342 (15.47%)
	Injection site induration	329 (14.88%)
	Peripheral oedema	8 (0.36%)
	Malaise	6 (0.27%)
	Chills	2 (0.09%)

[1]All changes (number of subjects and percentages) in the column of infants and/or toddlers are due to the addition of data from an infant study (670901).

[2] Originally, the concept Sleepiness, which comes from Study 99 MCIUK, was coded under the term Fatigue, while Drowsiness was covered under Sedation/Somnolence. This led to the situation where two concepts Fatigue and Sedation/Somnolence covered very similar conditions in infants and toddlers. To consolidate these similar conditions for all groups under one set of terms, Fatigue was added to Sedation/Somnolence.

Table 4 - Clinical Trial Adverse Reactions for Children (3.5 years to 18 years of age) (N=1911)

System Organ Class	ADR Term	Frequency (%)
Infections and infestations	Pharyngitis/Rhinitis	151 (9.21%)
Blood and lymphatic system disorders	Lymphadenopathy	8 (0.42%)
Immune system disorders	Hypersensitivity reaction (incl. bronchospasm)	11 (0.57%)
Metabolism and nutrition disorders	Decreased appetite	12 (0.63%)
Psychiatric disorders	Agitation/Restlessness	2 (0.10%)
Nervous system disorders	Headache	279 (14.60%)
	Dizziness	36 (1.88%)
	Sedation/somnolence/fatigue[1]	26 (1.36%)
	Sensory abnormalities (i.e., Paraesthesia, Burning sensation, Hypoesthesia)	13 (0.68%)
	Syncope	6 (0.31%)
	Crying	5 (0.26%)
	Convulsion	2 (0.10%)
Eye disorders	Eyelid oedema	2 (0.10%)
Vascular disorders	Flushing	6 (0.31%)
	Circulatory collapse	1 (0.05%)
Respiratory, thoracic and mediastinal disorders	Cough	42 (2.20%)
	Nasal congestion	6 (0.31%)
Gastrointestinal disorders	Nausea	99 (5.18%)
	Abdominal pain	64 (3.35%)
	Vomiting	30 (1.57%)
	Diarrhoea	20 (1.05%)
Skin and subcutaneous tissue disorders	Pruritus	44 (2.30%)
	Ecchymosis	39 (2.04%)
	Dermatitis	26 (1.36%)

Table 4 - Clinical Trial Adverse Reactions for Children (3.5 years to 18 years of age) (N=1911)		
System Organ Class	**ADR Term**	**Frequency (%)**
	Hyperhidrosis	7 (0.37%)
	Rash	3 (0.16%)
Musculoskeletal and connective tissue disorders	Pain in extremity	108 (5.65%)
	Musculoskeletal stiffness (incl. neck stiffness, joint stiffness)	18 (0.94%)
	Neck pain	10 (0.52%)
	Myalgia	6 (0.31%)
	Arthralgia	5 (0.26%)
	Back pain	3 (0.16%)
General disorders and administration site conditions	Injection site tenderness/pain	1145 (59.92%)
	Injection site erythema	639 (33.44%)
	Injection site swelling	465 (24.33%)
	Fever	80 (4.19%)
	Malaise	57 (2.98%)
	Fatigue	49 (2.56%)
	Irritability	15 (0.78%)
	Asthenia	8 (0.42%)
	Chills	6 (0.31%)
	Peripheral oedema	5 (0.26%)
	Influenza-like illness	1 (0.05%)

[1] Originally, the concept Sleepiness, which comes from Study 99 MCIUK, was coded under the term Fatigue, while Drowsiness was covered under Sedation/Somnolence. This led to the situation where two concepts Fatigue and Sedation/Somnolence covered very similar conditions in infants and toddlers. To consolidate these similar conditions for all groups under one set of terms, Fatigue was added to Sedation/Somnolence.

In infants and toddlers, and partially in children, NeisVac-C® has been administered concomitantly with one or two other routine multivalent pediatric vaccines. In some studies, NeisVac-C® and another vaccine were administered in the same limb. Therefore, the adverse reactions listed for the respective age groups, may represent a cumulative effect of the administration of these vaccines.

In a study (n=945) comparing two different single dose priming schedules (vaccinations at 4 or 6 months of age) with a two dose priming schedule (vaccinations at 2 and 4 months of age), local and systemic reactions occurred at comparable rates in the three study groups and were mainly of mild severity. An additional adverse reaction (very common) was induration at the injection site, with an overall frequency of 53.0%. Fever and sleep disorder were reported with an overall frequency of 54.9% and 34.8%, respectively in this study.

8.5 Post-Market Adverse Reactions

Table 5 - Post Marketing Adverse Drug Reaction Table	
System Organ Class	**Adverse Drug Reactions**
Blood and lymphatic system disorders	Idiopathic thrombocytopenic purpura
	Lymphadenopathy
Immune system disorders	Anaphylaxis
	Angioedema (incl. Facial oedema)

Table 5 - Post Marketing Adverse Drug Reaction Table	
System Organ Class	**Adverse Drug Reactions**
	Hypersensitivity reaction (incl. Bronchospasm)
Metabolism and nutrition disorders	Decreased appetite
Psychiatric disorders	Sleep disorder (incl. Impaired sleeping)
Nervous system disorders	Febrile convulsions
	Convulsion
	Meningism
	Hypotonic-hyporesponsive episode
	Syncope
	Dizziness
	Sensory abnormalities (incl. Paraesthesia, Burning sensation, Hypoesthesia)
	Hypersomnia
Respiratory, thoracic and mediastinal disorders	Apnoea
	Dyspnoea
	Wheezing
	Nasal congestion
Gastrointestinal disorders	Nausea
Skin and subcutaneous tissue disorders	Stevens-Johnson syndrome
	Erythema multiforme
	Petechiae
	Purpura
	Urticaria
	Rash (incl. Maculovesicular rash, Vesicular rash, Maculopapular rash, Papular rash, Rash macular, Heat rash, Rash erythematous, Rash generalized, Rash pruritic)
	Erythema
Musculoskeletal and connective tissue disorders	Musculoskeletal stiffness (incl. Neck stiffness, Joint stiffness)
	Neck pain
	Pain in extremity
General disorders and administration site conditions	Peripheral oedema
	Asthenia
	Fatigue
	Chills

9 DRUG INTERACTIONS

9.2 Drug Interactions Overview

NeisVac-C® vaccine (meningococcal group C-TT conjugate vaccine, adsorbed) must not be mixed with other vaccines in the same syringe. Separate injection sites should be used if more than one vaccine is being administered.

9.4 Drug-Drug Interactions

The vaccine can be administered safely at the same time as diphtheria, tetanus and whole cell or acellular pertussis-containing vaccines, e.g. DTP, Td, DT, Haemophilus influenzae type b conjugate

vaccines (Hib), measles, mumps and rubella vaccine (MMR), inactivated polio vaccine (IPV), pneumococcal conjugate vaccine (7- and 10- valent), or oral, live rotavirus vaccine.

NeisVac-C® vaccine administration did not affect antibody responses to diphtheria and tetanus toxoid, Hib conjugate vaccines or MMR.

Administration of meningitis group C-conjugate vaccine at the same time as, but at a separate injection site from, IPV, DTP, Hib, DTaP, DT, Td and MMR vaccines does not reduce the immunologic response to any of these other antigens.

Concomitant administration of NeisVac-C® vaccine (2 dose infant schedule) and INFANRIX hexa® (DTaP-IPV-HBV-Hib) in a 3-dose primary series in infants did not indicate any clinically relevant interference with responses to any of the antigens in the hexavalent vaccine.

Concomitant administration of NeisVac-C® with Prevnar®, a 7-valent pneumococcal conjugate vaccine, given in infants did not indicate any clinically relevant immunologic interference. Also, concomitant administration with SYNFLORIX®, a 10-valent pneumococcal conjugate vaccine did not reveal any evidence of immunologic interference between the two conjugate vaccines after the primary series or after the booster dose.

Concomitant administration of NeisVac-C® with an oral, live rotavirus vaccine (RotaTeq®) at 3 and 5 months of age (and usually at the same time as DTaP-IPV-Hib vaccine), followed by a third dose of the rotavirus vaccine at approximately 6 months of age, demonstrated that the immune responses to both vaccines were unaffected.

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

NeisVac-C® vaccine (meningococcal group C-TT conjugate vaccine, adsorbed) is intended for the prevention of meningitis and/or septicemia caused by *Neisseria meningitidis* group C in infants and older age groups. NeisVac-C® vaccine is composed of a meningococcal group C polysaccharide conjugated to a tetanus toxoid protein, a chemically detoxified form of tetanus toxin, adsorbed onto aluminum hydroxide.

In clinical trials, NeisVac-C® vaccine was shown to be highly immunogenic in infants, children, adolescents and adults against serogroup C *Neisseria meningitidis*. Immunologic memory was also demonstrated in all age groups (see 14 Clinical Trials).

10.2 Pharmacodynamics

No pharmacodynamics studies have been conducted with NeisVac-C® vaccine in accordance with its status as a vaccine.

10.3 Pharmacokinetics

No pharmacokinetics studies have been conducted with NeisVac-C® vaccine in accordance with its status as a vaccine.

11 STORAGE, STABILITY AND DISPOSAL

Store at 2°C to 8°C. Do not freeze. Do not use vaccine after expiration date.

Within the indicated shelf life the product may be stored at room temperature (up to +25°C) for a single period not exceeding 9 months. Record the period of storage at room temperature on the product package. At the end of this period, the product should be used or discarded.

12 SPECIAL HANDLING INSTRUCTIONS

The vaccine should be well shaken prior to use (see 4 DOSAGE AND ADMINISTRATION).

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: Meningococcal group C polysaccharide conjugated to tetanus toxoid.

Product Characteristics:
NeisVac-C® vaccine (meningococcal group C-TT conjugate vaccine, adsorbed) is a semi-opaque white to off-white suspension presented as a 0.5 mL latex-free pre-filled syringe. NeisVac-C® vaccine is composed of a meningococcal group C polysaccharide conjugated to a tetanus toxoid protein, a chemically detoxified form of tetanus toxin, adsorbed onto aluminum hydroxide.

14 CLINICAL TRIALS

Study Results

In six clinical trials performed in the various target age groups, NeisVac-C® vaccine was shown to be highly immunogenic and able to induce serum bactericidal activity (SBA) against meningococcal strain C11. The clinical trial data is summarized below.

In one clinical trial in infants 2 months of age, 100% of subjects achieved a SBA titre of at least 1/8 and 99% of subjects achieved a SBA titre of at least 1/16 after the first dose of NeisVac-C® vaccine at 4 weeks post-vaccination (see Table below). Following the second and third doses (at 3 and 4 months of age), 100% of infants had antibody titres of 1/16 and 98.7% had titres of at least 1/32. However, about 8-10 months following the primary vaccination, only 32-34% of subjects had antibody titres of 1/16. A booster vaccination with NeisVac-C® vaccine was given approximately 8 months after completion of the primary vaccination series. All children (n=24) from whom blood was drawn within 3-5 weeks after the booster achieved a SBA titre of at least 1/32.

Among infants 2 months of age in a second clinical trial, 98.4% achieved a SBA titre of at least 1/8, 96.7% achieved a SBA titre of at least 1/16 and 95.6% had titres of at least 1/32 after a single dose. Following a second dose at 4 months of age, 100% of infants had antibody titres of at least 1/8 and 1/16 and 99.5% had titres of at least 1/32. A polysaccharide challenge in the second year of life induces

an anamnestic response in both groups. Almost all infants received DTP-Hib and OPV concomitantly with NeisVac-C® vaccine.

Another clinical study (n=786) investigated the immune response to a single dose of NeisVac-C® given at 4 or 6 months of age as compared to that of two doses at 2 and 4 months of age, based on comparing proportion of subjects with rSBA titres[1] of at least 1:8. All children received a booster dose at 12-13 months of age. Among infants given a single dose of NeisVac-C® at either 4 months (n=271), or at 6 months of age (n=265), 99.6% and 99.2% achieved a rSBA titre of at least 1:8, respectively. Among infants given two doses of NeisVac-C® at 2 and 4 months of age (n=250), 99.6% achieved a rSBA titre of at least 1:8. Prior to the booster, 78.0% and 90.7% of subjects had seroprotective antibody titers in the single dose groups (month 4 or month 6, respectively), and 67.8% in the two-dose group. One month after the booster, 98.9% and 99.6% of subjects achieved a rSBA titre of at least 1:128 in the single dose groups (month 4 or month 6, respectively), and 99.6% in the two-dose group.

Among toddlers aged 12 to 17 months, 100% of individuals developed serum bactericidal antibody titres of at least 1/8 one month after a single dose of NeisVac-C® vaccine, and 97.2% had titres of at least 1/32. Additionally, a single dose in toddlers has been demonstrated to induce immunologic memory.

Among children, aged 3.5 to 6 years of age, 98.6% of individuals developed serum bactericidal antibody titres of at least 1/32 one month following vaccination.

Among adolescents aged 13 through 17 years, 100% of individuals developed serum bactericidal antibody titres of at least 1/32 one month following vaccination.

In one study on 30 adults (18 to 46 years of age), all developed serum bactericidal antibody titres of at least 1/32 one month after a single dose of NeisVac-C® vaccine. There are no data in adults aged 65 years and more.

The number of subjects for each relevant study and age group is presented in the following table, which provides a summary of immunological results.

[1] rSBA: rabbit complement serum bactericidal assay

Table 6 - Summary of immunological results						
Studies	**Number of volunteers achieving titre/total number of volunteers**					
	Titre ≥ 1:8*		**Titre ≥ 1:16***		**Titre ≥ 1:32***	
Infants						
Study 97-C002 (5)						
1 dose	71/71	(100%)	70/71	(98.6%)	68/71	(95.8%)
2 doses	79/79	(100%)	79/79	(100%)	78/79	(98.7%)
3 doses	75/75	(100%)	75/75	(100%)	75/75	(100%)
Booster dose			24/24	(100%)	24/24	(100%)
Infants						
Study 99MCIUK (6)						
1 dose	179/182	(98.4%)	176/182	(96.7%)	174/182	(95.6%)
2 doses	188/188	(100%)	188/188	(100%)	187/188	(99.5%)
3 doses	172/173	(99.4%)	172/173	(99.4%)	170/172	(98.8%)
Infants						
Study 670901 (7)						
1 dose (4 months)	270/271	(99.6%)*				
1 dose (6 months)	263/265	(99.2%)*				
2 doses (2 and 4 months)	249/250	(99.6%)*				
Booster dose	>98.9%**					
Studies in older age groups						
Toddlers						
Study MCT-9701 (8)	72/72	(100%)	71/72	(98.6%)	70/72	(97.2%)
Children						
Study MCPSB-9701 (9)	72/73	(98.6%)	72/73	(98.6%)	72/73	(98.6%)
Adolescents						
Study MCSL-9702 (9)	28/28	(100%)	28/28	(100%)	28/28	(100%)
Adults						
Study 94-C001 (10)	30/30	(100%)	30/30	(100%)	30/30	(100%)

Blood draw for serology was done approximately 4 weeks after vaccination.
*Serum bactericidal activity (rSBA) titres against meningococcal strain C11
**>98.9 % of infants in all three groups achieved rSBA titres > 1:128

Estimates of vaccine effectiveness from a routine immunization programme in the UK (using various meningococcal serogroup C conjugate vaccines) covering the period from introduction at the end of 1999 to March 2004 have demonstrated the need for a booster dose after completion of the primary series (administered at 2, 3 and 4 months). Within one year of completion of the primary series, vaccine effectiveness in the infant cohort was estimated at 93% (95% CI 67%; 99%). However, more than one year after completion of the primary series, there was clear evidence of waning protection.

Up to 2007 the overall estimates of effectiveness in age cohorts from 1-18 years that received a single dose of meningococcal group C conjugate vaccine during the initial catch-up vaccination programme in the UK range between 83 and 100%. The data show no significant decrease in effectiveness within these age cohorts when comparing time periods less than a year or one year or more since immunization.

In September 2002, the Netherlands implemented routine meningococcal group C vaccination for toddlers at 14 months of age. In addition, between June and November 2002, a catch-up campaign from 1-18 years of age was carried out. Disease surveillance in the Netherlands where NeisVac-C® has been used exclusively in the vaccination programmes, revealed that the incidence of meningococcal C

disease has decreased sharply, and up to 2012 no cases of meningococcal C disease had been reported in subjects previously vaccinated with NeisVac-C®.

Formal protective efficacy studies have not been performed.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

Animal immunogenicity: Various immunogenicity studies were conducted in mice to evaluate optimization of chemical modification of the polysaccharide (de-O-acetylation), dose, primary immunization schedule, the protein conjugate used and aluminum adjuvant types. These studies established the effectiveness of the current formulation using assays to detect meningococcal group C-specific IgG and complement-dependent serum bactericidal antibody in mouse serum.

General Toxicology: No significant systemic toxicity was observed in rats when 3 doses of NeisVac-C® vaccine (meningococcal group C-TT conjugate vaccine, adsorbed) were administered at 200-fold the human dose on a dose/weight basis. Full histological examination of the reproductive organs has shown no adverse effect on these organs in either the male or female rats examined. However, no reproductive data are currently available.

An extensive program of preclinical immunogenicity testing in rodent and non-rodent models, including non-human primates, has demonstrated an absence of acute or delayed adverse reaction to the injection of NeisVac-C® vaccine. Safety assessment was thus originally derived from studies of immunogenicity. General safety and pyrogenicity studies have been performed, including a full-spectrum repeat-dose toxicity study in rats for NeisVac-C® vaccine.

The general safety assays of NeisVac-C® vaccine batches were performed using both mouse and guinea pig models. These studies showed evidence of the absence of toxic reactions following intraperitoneal injection: there were no signs of pharmacological action that would indicate any effect on the cardiovascular or central nervous systems, either direct or by secondary messenger.

In addition, results of pyrogenicity assays demonstrated the absence of toxic effects of potential impurities derived from bacteria.

The repeat-dose toxicity study was performed using three high-dose (approximately 2-fold human dose or 200-fold the human dose on a mg/kg basis) intramuscular injections at 2-week intervals in groups of 10 male and 10 female Sprague-Dawley rats, beginning at 6 weeks of age. The study monitored the clinical conditions, body weight, food consumption, ophthalmology, hematology and urinalysis, coagulation, serum clinical chemistry and serology, necropsy, and organ weight with a full-spectrum, terminal histopathological examination of all animals. Administration of the three injections of NeisVac-C® vaccine (20 mcg polysaccharide per dose) induced a strong functional antibody response in all animals and a memory response close to maximum after the second injection. The protein carrier response continued to rise steeply with the third injection. There were no changes in mean organ weights. All rats survived to terminal necropsy. No significant systemic toxicity was observed in rats when NeisVac-C® vaccine was administered at maximal feasible dose level. Histopathological examination showed no adverse effect on reproductive organs in male or female rats. The local tolerance of NeisVac-C® vaccine was marginally better than the control vaccine (PedvaxHIB®).

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

NEISVAC-C® VACCINE

Meningococcal Group C-TT Conjugate Vaccine, Adsorbed

Read this carefully before you start taking **NeisVac-C® vaccine** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **NeisVac-C® vaccine**.

Serious Warnings and Precautions

- **NeisVac-C® vaccine** should under no circumstances be injected intravenously or subcutaneously.

What is NeisVac-C® vaccine used for?

NeisVac-C® vaccine is one of a general group of medicines called vaccines, which are used to protect against infectious diseases. NeisVac-C® vaccine is used to prevent disease caused by bacteria called *Neisseria meningitidis* group C. The vaccine works by causing the body to produce its own protection (antibodies) against the group C bacteria.

The *Neisseria meningitidis* group C bacteria can cause serious and sometimes life-threatening infections such as meningitis and septicaemia (blood poisoning).

NeisVac-C® vaccine will only protect against disease caused by the meningococci group C bacteria. It will not protect against infections caused by other groups of meningococci or other organisms that cause meningitis and blood poisoning. As with other vaccines, NeisVac-C® vaccine cannot completely prevent meningococcal group C infections in all people who are vaccinated.

How does NeisVac-C® vaccine work?

NeisVac-C® vaccine works by causing your body to produce its own protection (or antibodies), against these types of meningococcal bacteria. NIMENRIX cannot cause meningococcal disease.

What are the ingredients in NeisVac-C® vaccine?

One dose (0.5 mL) of the vaccine contains the following:
Medicinal ingredients: *Neisseria meningitidis* group C polysaccharide conjugated, tetanus toxoid protein absorbed on aluminium hydroxide
Non-medicinal ingredients: sodium chloride and water for injection

NeisVac-C® vaccine comes in the following dosage forms:

The NeisVac-C® vaccine is a suspension for injection packaged in pre-filled syringes of 10 mcg meningococcal group C-TT conjugate vaccine, adsorbed.

Do not use NeisVac-C® vaccine if:

You or your child are allergic to the active substance or any of the other ingredients of this vaccine.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take NeisVac-C® vaccine. Talk about any health conditions or problems you may have, including if

you:

- Have you ever had an allergic reaction (for example, symptoms such as itchy generalized skin rash, swelling of the face and throat, difficulty in breathing, blue discolouration of the tongue or lips, low blood pressure and collapse) to any ingredient of the vaccine including tetanus toxoid?
- Have you ever had an allergic reaction to any other vaccine intended to protect against meningococcal group C infections?
- Have an infectious illness (for example, high temperature, sore throat, cough, cold or flu)?
- Have hemophilia or any other problem that may stop your blood from clotting properly
- Have been told that you have a weak immune system for any reason? For example, have you been told that you do not produce antibodies very efficiently or that you have a complement deficiency, or are you taking medicines that reduce your immunity to infections (such as anti-cancer drugs, radiation therapy, eculizumab or high doses of corticosteroids)?
- Have had your spleen removed or been told that your spleen does not work as it should
- You over 65 years old

Other warnings you should know about:

In babies born very prematurely (at or before 28 weeks of gestation) longer gaps than normal between breaths may occur for 2-3 days after vaccination. Parents are advised to contact their physician, if any abnormal breathing is noticed.

Breastfeeding and pregnancy

- Are you pregnant, planning to become pregnant or breastfeeding? NeisVac-C® vaccine may still be given to you by a doctor or nurse if the risk of infection is considered to be high.

Driving and operating machinery

- The vaccine is unlikely to affect your ability to drive or operate machinery.

Although this vaccine contains tetanus toxoid, it does not reliably protect you against tetanus (lockjaw). Therefore, routine vaccines against tetanus should still be given when they are due (your doctor or nurse will advise you when you need vaccination against tetanus).

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

Although there are no known interactions with other medicines, you should tell your doctor or nurse about any other medicines which you are taking, whether prescribed or bought without prescription.

Your doctor or nurse will advise you if you should need to have NeisVac-C® vaccine at the same time as other injected vaccines.

NeisVac-C® vaccine may be given at the same time as, but as separate injections at different injection sites from vaccines that protect against polio, measles, mumps, and rubella (MMR), diphtheria, tetanus and pertussis (whooping cough), infections caused by Haemophilus influenzae (Hib), pneumococcal infections, and rotavirus infections.

NeisVac-C® vaccine can be given to infants at the same time as certain types of vaccines that protect against hepatitis B infection. Your doctor will advise you if this is necessary and which vaccine might be suitable.

How to take NeisVac-C® vaccine:

The NeisVac-C® vaccine is usually injected into the muscle of the arm (in children from the age of 12 months and older persons) or thigh (in children from two months old up to the age of 12 months). In children 12 to 24 months of age, the vaccine may be administered in the muscle of the arm or the thigh. The vaccine must not be injected under the skin or into a blood vessel and your doctor or nurse will take care to avoid doing so when administering the vaccine.

Usual dose:
One dose of NeisVac-C® vaccine is 0.5 mL (half a millilitre – a very small amount of liquid).

Your child may receive one or two injections before they are 12 months old, and another injection at approximately 12 to 13 months of age, with an interval of at least 6 months after last NeisVac-C® vaccination.

Older children (12 months and older), adolescents and adults will receive one injection only.

Overdose:

An overdose is highly unlikely to happen because it is administered from a single-dose syringe by a doctor or nurse.

If you think you, or a person you are caring for, have taken too much NeisVac-C® vaccine, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

Missing a dose is highly unlikely, since it is administered as a single dose by a health care provider.

What are possible side effects from using NeisVac-C® vaccine?

These are not all the possible side effects you may have when taking NeisVac-C® vaccine. If you experience any side effects not listed here, tell your healthcare professional.

This vaccine cannot cause meningococcal group C disease. If you or your child experiences neck pain, neck stiffness or a dislike of light (photophobia), drowsiness or confusion, or red or purple bruise-like spots that do not fade under pressure you should contact your doctor or local Hospital Emergency Department immediately to rule out other causes.

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
VERY COMMON			
Injection site reactions / redness, swelling, hardening at the site of injection, and tenderness, pain at the injection site	x		
Headaches and fever	x		

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
In Infants: loss of appetite, feeling or being sick, vomiting and diarrhea	x		
In Infants: crying, irritability	x		
In Infants: drowsiness and sleepiness, or impaired sleeping	x		
COMMON			
Fever	x		
Muscle pain and pains in the arms or legs	x		
Drowsiness and sleepiness, or impaired sleeping	x		
In older children: loss of appetite, feeling or being sick or diarrhea	x		
RARE			
serious allergic reactions / swelling of the lips, mouth, throat, rash and swelling of the hands, feet and ankles]			x
severe skin rashes / itching, hives and other rashes			x
Fits /seizures			x
VERY RARE			
swollen lymph glands	x		
dizziness, faints	x		
abnormal or reduced sensation		x	
loss of muscle tone or floppiness in infants			x
purple spots or blotches under the skin and may look like bruises	x		

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Suspected Side Effects for Vaccines

For the general public: Should you experience a side effect following immunization, please report it to your healthcare professional.

Should you require information related to the management of the side effect, please contact your healthcare professional. The Public Health Agency of Canada, Health Canada and [Sponsor Name] cannot provide medical advice.

For healthcare professionals: If a patient experiences a side effect following immunization, please complete the Adverse Events Following Immunization (AEFI) Form appropriate for your province/territory (http://www.phac-aspc.gc.ca/im/aefi-essi-form-eng.php) and send it to your local Health Unit.

Storage:

This medicine should be stored in the refrigerator at +2°C to +8°C (Do Not Freeze). The product may be taken out of the refrigerator and stored at room temperature for a single period of not more than 9 months, as long as this time period ends before the expiry date written on the label. The date that the product is taken out of the refrigerator should be written on the box in the space provided. If the product has not been used within 9 months of the date it was taken out of the refrigerator (or by the expiry date, whichever is sooner), the product should be discarded.

The vaccine should be used before the expiry date printed on the label.

Keep out of reach and sight of children.

If you want more information about NeisVac-C® vaccine:

- Talk to your healthcare professional

Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website www.pfizer.ca, or by calling -800-463-6001 (Medical Information).

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