

PRODUCT MONOGRAPH

NeisVac-C[®] Vaccine

Meningococcal Group C-TT Conjugate Vaccine, Adsorbed

Suspension for Injection

Active Immunizing Agent

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NeisVac-C[®] Vaccine

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PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
Intramuscular	Suspension for injection/ 10 mcg <i>Neisseria meningitidis</i> group C polysaccharide*	Aluminum hydroxide. <i>For a complete listing see Dosage Forms, Composition and Packaging section.</i>

* Conjugated to tetanus toxoid carrier protein

DESCRIPTION

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.

INDICATIONS AND CLINICAL USE

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.

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

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 DOSAGE FORMS, COMPOSITION AND PACKAGING).

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

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

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.

Non-conjugated meningococcal polysaccharide vaccines should not be used for booster vaccination as they may negatively influence the immunologic memory.⁽¹⁾

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.

Special Populations

Pregnant and Nursing 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.

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

ADVERSE REACTIONS

Adverse Drug 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); anorexia, vomiting, nausea or diarrhea, crying and irritability (in infants and/or toddlers); anorexia, 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.⁽²⁾

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

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.

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 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, anorexia, 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 myalgia in adults (1 in 100) and irritability (ranging from 1 in 2 babies to 1 in 25 pre-school children) and somnolence in younger children.

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

Frequency of Adverse Reactions (AR)	Adverse Reaction (Percent of Subjects with AR*)
Very Common (more than 10%)	Injection site reactions: redness (5-50%) tenderness/pain (14-71%) swelling (8-31%) Pain in limb (32%) Headache (7-26%) Crying and irritability in infants and toddlers (22-53%) Drowsiness/somnolence/impaired sleeping in infants and toddlers (12-53%) Vomiting/nausea/diarrhea in infants (12%) Loss of appetite in infants (27%)
Common (between 1% and 10%)	Fever (1-7%) Loss of appetite in children (1-7%) Vomiting/nausea/diarrhea in children (3-5%) Muscle pain in older children and adults (6-7%) Pain in limb in children (2%) Drowsiness/somnolence/impaired sleeping (3-8%)

* The range of AR frequency percentages in clinical studies is provided for each AR. Percentages are based on all age groups unless otherwise stated.

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 in the table above, 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) which is not included in the adverse reactions table presented above, but was reported in this study, 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.

Post-Market Adverse Drug Reactions (for all age groups)

The following additional undesirable effects were reported under the spontaneous reporting system:

Blood and Lymphatic System Disorders:

Lymphadenopathy, idiopathic thrombocytopenic purpura

Immune System Disorders:

Anaphylaxis, hypersensitivity reactions including bronchospasm, facial oedema and angioedema.

Nervous System Disorders:

Dizziness, convulsions including febrile convulsions, faints, hypoaesthesia, and paraesthesia, hypotonia in infants.

There have been very rare reports of seizures following meningococcal group C conjugate vaccine administration. Individuals have usually rapidly recovered. Some of the reported seizures may have been faints. The reporting rate of seizures was below the background rate of epilepsy in children. In infants, seizures were usually associated with fever and were likely to be febrile convulsions.

Respiratory, Thoracic and Mediastinal Disorders:

Apnea in very premature infants (≤ 28 weeks of gestation).

Gastrointestinal Disorders:

Vomiting and nausea.

Skin and Subcutaneous Tissue Disorders:

Rash, urticaria and pruritus.

Stevens-Johnson syndrome and erythema multiforme have been reported in post-marketing surveillance for other Meningococcal Group C Conjugate Vaccines.

Very rarely petechiae and/or purpura have been reported following vaccination. However, new cases should be investigated for aetiology as recommended under WARNINGS AND PRECAUTIONS.

Musculoskeletal, Connective Tissue and Bone Disorders:

Arthralgia.

Renal Disorders:

Relapse of nephrotic syndrome has been reported in association with meningococcal group C conjugate vaccines.⁽¹⁾

All adverse drug reaction reports received under spontaneous reporting conditions (post-marketing surveillance) were at a frequency of very rare ($<0.01\%$) except for the adverse drug reaction of rash which has been a rarely (between $\geq 0.01\%$ and $<0.1\%$) reported event.

DRUG INTERACTIONS

Drug-Drug Interactions

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.

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.

DOSAGE AND ADMINISTRATION

Recommended Dose and Dosage Adjustment

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.

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 CLINICAL TRIALS).⁽³⁾

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 CLINICAL TRIALS).

Administration

The vaccine must not be administered subcutaneously or intravenously.

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.

OVERDOSAGE

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

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.⁽⁵⁾

ACTION AND CLINICAL PHARMACOLOGY

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 CLINICAL TRIALS).

Pharmacodynamics/Pharmacokinetics

No pharmacodynamics studies and no pharmacokinetics studies have been conducted with NeisVac-C[®] vaccine in accordance with its status as a vaccine.

STORAGE AND STABILITY

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.⁽⁴⁾ 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.

SPECIAL HANDLING INSTRUCTIONS

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

DOSAGE FORMS, COMPOSITION AND PACKAGING

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.

One dose 0.5 mL contains:

<i>Neisseria meningitidis</i> group C polysaccharide	10 mcg
tetanus toxoid	10-20 mcg
aluminum hydroxide	0.5 mg Al ³⁺
sodium chloride	4.1 mg

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

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

Meningococcal group C polysaccharide conjugated to tetanus toxoid.

CLINICAL TRIALS

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.⁽⁵⁾ 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.⁽⁶⁾

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 titres¹ 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%

¹ rSBA: rabbit complement serum bactericidal assay

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.⁽⁷⁾

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.⁽⁸⁾

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.⁽⁹⁾

Among adolescents aged 13 through 17 years, 100% of individuals developed serum bactericidal antibody titres of at least 1/32 one month following vaccination.⁽⁹⁾

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.⁽¹⁰⁾ 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.

Study	Number of volunteers achieving titre/total number of volunteers		
	Titre ≥ 1:8*	Titre ≥ 1:16*	Titre ≥ 1:32*
Infants <u>Study 97-C002</u> (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 <u>Study 99MCIUK</u> (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 <u>Study 670901</u> (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[®].⁽¹¹⁾

Formal protective efficacy studies have not been performed.

DETAILED PHARMACOLOGY

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.

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, haematology 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[®]).

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PART III: CONSUMER INFORMATION

NeisVac-C[®] Vaccine

Meningococcal Group C-TT Conjugate Vaccine, Adsorbed

This leaflet is Part III of a three-part "Product Monograph" published when NeisVac-C[®] vaccine was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about NeisVac-C[®] vaccine. Contact your doctor or pharmacist if you have any questions about NeisVac-C[®] vaccine.

Please read this leaflet carefully before receiving NeisVac-C[®] vaccine as it contains information about your vaccine. It may be useful to keep this leaflet in case you need to read it again after vaccination.

ABOUT THIS MEDICATION

What is NeisVac-C[®] Vaccine and What Does It Do?

The name of the vaccine is NeisVac-C[®] vaccine (meningococcal group C-TT conjugate vaccine, adsorbed) and is a suspension for injection packaged in pre-filled syringes.

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.

What Is In Your Medication?

One dose (0.5 mL) of the vaccine contains, as the active ingredient, 10 micrograms of *Neisseria meningitidis* group C polysaccharide conjugated with (joined to) 10 to 20 micrograms of tetanus toxoid protein, adsorbed on 0.5 mg aluminium hydroxide.

The other ingredients in NeisVac-C[®] vaccine are sodium chloride and water for injection.

What Dosage Forms Does Your Medication Come In?

NeisVac-C[®] vaccine is supplied as a suspension for injection in pre-filled syringes.

WARNINGS AND PRECAUTIONS

NeisVac-C[®] vaccine should not be given if the answer to the following question is "YES" for the person receiving the injection.

- 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?

NeisVac-C[®] vaccine may not be suitable for you if the answer to the following question is "YES". Your doctor or nurse will decide if you may receive NeisVac-C[®] vaccine.

- Have you ever had an allergic reaction to any other vaccine intended to protect against meningococcal group C infections?

NeisVac-C[®] vaccine may have to be delayed if the answer to the following question is "YES" for the person receiving the injection.

- Do you have an infectious illness (for example, high temperature, sore throat, cough, cold or flu)?

Take special care with NeisVac-C[®] vaccine.

If the answer to any of the following questions is "YES" for the person receiving the injection, talk with your doctor or nurse before having this vaccine as it may not be suitable. In some instances, you may still be given the vaccine but it may not provide very high protection against infections caused by the group C bacteria.

- Do you have haemophilia or any other problem that may stop your blood from clotting properly?
- Have you 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 are you taking medicines that reduce your immunity to infections (such as anti-cancer drugs or high doses of corticosteroids)?
- Have you had your spleen removed or been told that your spleen does not work as it should?
- Are you over 65 years old?

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).

INTERACTIONS WITH THIS MEDICATION

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.

PROPER USE OF THIS MEDICATION

Usual Dose

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

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

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

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

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

As with all medicines, NeisVac-C[®] vaccine may cause side effects in some persons. If any side effects worry you, or you have any unusual symptoms, please contact your doctor, nurse or pharmacist. Side effects occurring in more than 1 in 10 people are considered to be very common. Those that occur in more than 1 in 100 people but less than 1 in 10 are considered to be common, and side effects occurring in fewer than 1 in 10,000 people are considered to be very rare.

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in cases of very rare but serious allergic reactions.

Symptoms of serious allergic reactions include: swelling of the lips, mouth, throat (which may cause difficulty in swallowing or breathing), sometimes accompanied by a rash and swelling of the hands, feet and ankles. Symptoms of allergic reactions may also include drops in blood pressure and unconsciousness. When these signs or symptoms occur they usually develop very quickly after the injection is given and while the person affected is still in the clinic or doctor's office. If any of these symptoms occur after leaving the place where your injection was given, you must consult a doctor IMMEDIATELY.

Very rarely, severe skin rashes can occur that can cover much of the body and lead to blistering and peeling. The inside of the mouth and the eyes can also be affected. Less severe allergic reactions include itching, hives and other rashes.

Fits (seizures) have been reported very rarely after vaccination including some fits in people who already had fits at times. In teenagers and adults, some of the reports of fits may actually have been fainting attacks. In infants and young children seizures were usually associated with fever

and were likely to be febrile convulsions. Most people recovered rapidly after the fit.

Injection site reactions are very common side effects in all age groups and include redness, swelling, hardening at the site of injection, and tenderness/pain at the injection site. Headaches and fever are also very common.

Other very common side effects in infants and/or toddlers are loss of appetite, feeling or being sick and diarrhea, crying, irritability, drowsiness and sleepiness, or impaired sleeping.

Muscle pain and pains in the arms or legs are common or very common in older children and adults.

Common side effects in older children are loss of appetite, feeling or being sick or diarrhea

Very rare side effects include swollen lymph glands, dizziness, faints, abnormal or reduced sensation, loss of muscle tone or floppiness in infants, and purple spots or blotches under the skin which may be caused by a drop in special blood cells responsible for clotting and may look like bruises.

If you have previously been told by your doctor that you suffer from nephrotic syndrome (a kidney disease which may result in swelling, particularly around the face or eyes, protein in the urine making it appear frothy and/or weight gain) there may be an increased chance that this condition will reoccur within a few months after vaccination. You should tell your doctor if you notice similar symptoms after vaccination.

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.

If you notice any other side effects not mentioned in this leaflet, please inform your doctor, nurse or pharmacist.

HOW TO STORE IT

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 the sight and reach of children.

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

E-mail: 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 side effects, 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 can be obtained by contacting the sponsor, Pfizer Canada Inc., at: 1-800-463-6001 (Medical Information).

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