

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

NeisVac-C 0.5 ml Suspension for injection in pre-filled syringe.
Meningococcal Group C Polysaccharide Conjugate Vaccine Adsorbed.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose (0.5 ml) contains:

Neisseria meningitidis group C (strain C11) polysaccharide (de-O-acetylated)...10 micrograms
conjugated to tetanus toxoid.....10-20 micrograms
adsorbed on aluminium hydroxide, hydrated.....0.5 mg Al³⁺

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Suspension for injection in pre-filled syringe.
A semi-opaque white to off-white suspension.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

NeisVac-C is indicated for active immunisation in children from 2 months of age, adolescents and adults, for the prevention of invasive disease caused by *Neisseria meningitidis* serogroup C.

The use of NeisVac-C should be determined on the basis of official recommendations.

4.2 Posology and method of administration

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.

Posology

Primary immunisation

Infants from 2 months up to 4 months of age:
Two doses, each of 0.5 ml, should be given with an interval of at least two months
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 12-13 months of age with at least an interval of 6 months after the last NeisVac-C vaccination.
The need for booster doses in subjects aged 12 months or more when first immunised has not yet been established (see section 5.1).

Method of administration

NeisVac-C 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.

Precautions to be taken before handling or administering the medicinal product

The vaccine must not be administered subcutaneously or intravenously (see section 4.4).

NeisVac-C 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 (see section 4.5).

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1, including tetanus toxoid.

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

4.4 Special warnings and precautions for use

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.

NeisVac-C SHOULD UNDER NO CIRCUMSTANCES BE INJECTED INTRAVENOUSLY OR SUBCUTANEOUSLY.

Because of the risk of bleeding or hematoma at the injection site, benefits and risks should be carefully weighed when considering use of the vaccine in individuals with any coagulation disorder (e.g., thrombocytopenia) or concomitant anticoagulant therapy.

The potential risk of apnoea and the need for respiratory monitoring for 48-72 h should be considered when administering the primary immunisation 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.

This medicinal product contains less than 1 mmol sodium (23 milligrams) per dose, i.e. essentially “sodium-free”.

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

The benefit-risk assessment of vaccination with NeisVac-C depends on the incidence of *N. meningitidis* serogroup C infection in a given population before the institution of a widespread immunisation programme.

Vaccination should be postponed in subjects with acute clinical conditions (with or without fever) that could be aggravated by adverse reactions to the vaccine or could impair the interpretation of possible adverse reactions to the vaccine.

In subjects deficient in producing antibody (e.g. due to genetic defect 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 individuals with complement deficiencies and individuals with functional or anatomical asplenia would mount an immune response to meningococcal C conjugate vaccines; however, the degree of protection that would be afforded is unknown.

Although symptoms of meningism such as neck pain/stiffness or photophobia have been reported there is no evidence that meningococcal group C conjugate vaccines cause meningococcal C meningitis. Clinical alertness to the possibility of co-incidental meningitis should therefore be maintained.

This vaccine does not substitute for routine tetanus immunisation.

NeisVac-C 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. In the event of petechiae and/or purpura following vaccination (see section 4.8), the aetiology should be thoroughly investigated. Both infective and non-infective causes should be considered.

There are no data on the use of NeisVac-C in adults aged 65 years or more (see section 5.1).

4.5 Interaction with other medicinal products and other forms of interaction

NeisVac-C 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.

Administration of NeisVac-C at the same time (but into a different injection site) as vaccines containing the following antigens did not have a potentially clinically significant effect on immune responses to these antigens in clinical trials:

- diphtheria and tetanus toxoids
- whole cell pertussis vaccine (wP)
- acellular pertussis vaccine (aP)
- Haemophilus influenzae conjugate vaccine (Hib)
- inactivated polio vaccine (IPV)
- measles, mumps and rubella vaccine (MMR)
- pneumococcal conjugate vaccines (7-, 10-, and 13-valent)

Minor variations in geometric mean antibody levels were sometimes observed between concomitant and separate administrations but the clinical significance, if any, of these observations is not established.

Concomitant administration of NeisVac-C (2 dose infant schedule) and 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.

In various studies with different vaccines, concomitant administration of meningococcal serogroup C conjugates with combinations containing acellular pertussis components (with or without inactivated polio viruses, hepatitis B surface antigen or Hib conjugates) has been shown to result in lower SBA GMTs compared to separate administrations or to co-administration with whole cell pertussis vaccines. The proportions reaching SBA titres of at least 1:8 or 1:128 are not affected. At present, the potential implications of these observations for the duration of protection are not known.

The antibody response rate to NeisVac-C, when given one month after tetanus toxoid containing vaccine, was 95.7% as compared to 100% when vaccines were administered concurrently.

Co-administration of an oral, live rotavirus vaccine (RotaTeq vaccine) with NeisVacC 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. Co-administration resulted in an acceptable safety profile.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no adequate data from the use of this vaccine in pregnant women. Animal studies are insufficient with respect to the effects on pregnancy and embryonal/foetal development, parturition, and postnatal development. The potential risk for humans is unknown. Nevertheless, considering the severity of meningococcal C disease, pregnancy should not preclude vaccination when the risk of exposure is clearly defined.

Breast-feeding

There are no adequate data from the use of this vaccine in lactating women. The risk-benefit relationship should be examined before making the decision as to whether to immunise during lactation.

Fertility

The effects of NEISVAC-C on fertility have not been established.

4.7 Effects on ability to drive and use machines

The vaccine is unlikely to impair the ability to drive or operate machinery.

4.8 Undesirable effects

Tabulated summary of the safety profile

Adverse reactions from clinical studies

The following adverse reactions as listed below have been identified from clinical studies conducted with NeisVac-C in infants/toddlers 2 to <18 months of age (n=1266), in children 3.5 years to <18 years of age (n=1911) and in adults (n=130).

ADR frequency in clinical studies is based upon following scale:

Very common (>1/10); Common (>1/100-<1/10), Uncommon (>1/1000-<1/100), Rare (>1/10.000-<1/1000)

Frequency	System organ class (SOC)	Clinical trial adverse reaction		
		Infants /Toddlers 2 to <18 months of age	Children 3.5 to <18 years of age	Adults
Very common	METABOLISM AND NUTRITION DISORDER	Decreased appetite		
	NERVOUS SYSTEM DISORDERS	Crying, Sedation/Somnolence	Headache	Headache
	GASTROINTESTINAL DISORDERS	Vomiting		
	GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	Irritability, Fatigue*, Fever Injection site reactions including tenderness/pain, swelling and erythema	Injection site reactions including tenderness/pain, swelling and erythema	Injection site reactions including tenderness/pain, swelling and erythema
Common	INFECTIONS AND INFESTATIONS	Pharyngitis/Rhinitis	Pharyngitis/Rhinitis	
	PSYCHIATRIC DISORDERS	Agitation/Restlessness, Sleep disorder (impaired sleeping)		
	NERVOUS SYSTEM DISORDERS		Dizziness, Sedation/Somnolence	
	RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	Cough	Cough	
	GASTROINTESTINAL DISORDERS	Diarrhea	Nausea, Abdominal pain, Vomiting, Diarrhea	Vomiting
	SKIN AND SUBCUTANEOUS TISSUE DISORDERS	Rash, Hyperhidrosis	Pruritus, Ecchymosis, Dermatitis	
	MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS		Pain in extremity	Myalgia
	GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS		Fever, Malaise, Fatigue	Malaise, Fever
	BLOOD AND LYMPHATIC SYSTEM DISORDERS		Lymphadenopathy	Lymphadenopathy

Uncommon	IMMUNE SYSTEM DISORDERS		Hypersensitivity reaction (including bronchospasm)	
	METABOLISM AND NUTRITION DISORDERS		Decreased appetite	
	PSYCHIATRIC DISORDERS		Agitation/Restlessness	
	NERVOUS SYSTEM DISORDERS		Sensory abnormalities (i.e., paresthesia, burning sensation, hypoesthesia), Syncope, Crying, Convulsion	
	EYE DISORDERS		Eyelid edema	
	VASCULAR DISORDERS	Flushing	Flushing	
	RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS		Nasal congestion	
	GASTROINTESTINAL DISORDERS	Abdominal pain, Dyspepsia		
	SKIN AND SUBCUTANEOUS TISSUE DISORDERS	Erythema	Hyperhidrosis, Rash	
	MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	Pain in extremity	Musculoskeletal stiffness (including neck stiffness, joint stiffness), Neck pain, Myalgia, Arthralgia, Back pain	
	GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	Peripheral edema, Malaise, Chills	Irritability, Asthenia Peripheral edema, Chills	Influenza-like illness
Rare	IMMUNE SYSTEM DISORDERS	Hypersensitivity reaction (including bronchospasm)		
	EYE DISORDERS	Eyelid edema		
	VASCULAR DISORDERS	Circulatory collapse	Circulatory collapse	
	SKIN AND SUBCUTANEOUS TISSUE DISORDERS	Ecchymosis		
	MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	Musculoskeletal stiffness (including neck stiffness, joint stiffness)		
	GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS		Influenza-like illness	

* For infants and toddler see System organ class “Nervous System Disorders”

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. Two ADRs, which are not included in the ADR table presented above, were reported in this study: induration at the injection site and dermatitis, with an overall frequency of 53.0% and 0.2% , respectively.

Post-marketing experience

The following adverse reactions as described in the table below were reported during post marketing experience. Frequencies are not known as they cannot be estimated from the available data.

<i>System organ class (SOC)</i>	<i>Type of reaction</i>
BLOOD AND LYMPHATIC SYSTEM DISORDERS	Idiopathic thrombocytopenic purpura, Lymphadenopathy
IMMUNE SYSTEM DISORDERS	Anaphylaxis, Angioedema (including Facial edema), Hypersensitivity reaction (including Bronchospasm)
METABOLISM AND NUTRITION DISORDERS	Decreased appetite
PSYCHIATRIC DISORDERS	Sleep disorder (including Impaired sleeping)
NERVOUS SYSTEM DISORDERS	Febrile convulsions, Convulsion, Meningism, Hypotonic-hyporesponsive episode, Syncope, Dizziness, Sensory abnormalities (including Paresthesia, Burning sensation, Hypoesthesia), Hypersomnia
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	Apnea, Dyspnea, Wheezing, Nasal congestion
GASTROINTESTINAL DISORDERS	Nausea
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	Stevens-Johnson syndrome, Erythema multiforme, Petechiae, Purpura, Urticaria, Rash*, Erythema
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	Musculoskeletal stiffness (including Neck stiffness, Joint stiffness), Neck pain, Pain in extremity
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	Peripheral edema, Asthenia, Fatigue, Chills

*** including Maculovesicular rash, Vesicular rash, Maculopapular rash, Papular rash, Rash macular, Heat rash, Rash erythematous, Rash generalized, Rash pruritic**

Class reaction

Relapse of nephrotic syndrome has been reported in association with meningococcal group C conjugate vaccines in children

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via IMB Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.imb.ie; e-mail: imbpharmacovigilance@imb.ie.

4.9 Overdose

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

Multiple doses: in a 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 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Meningococcal vaccine

ATC code: J07AH

No clinical efficacy studies have been performed.

The serum bactericidal antibody (SBA) assay referenced in the text below used rabbit serum as a source of complement and strain C11.

Immunogenicity in Infants

A 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. All children received a booster dose at 12-13 months of age.

Proportion of Subjects with Seroprotective antibody titers			
Schedule	post primary (rSBA ≥ 8)*	pre booster (rSBA ≥ 8)**	post booster (rSBA ≥128)*
	90 % CI	90 % CI	90 % CI
Single dose	99,6 %	78,9 %	98,9 %
at 4 mo	98,3 – 100,0	73,4 – 82,2	97,1 – 99,7
Single dose	99,2 %	90,7 %	99,6 %
at 6 mo	97,6 – 99,9	87,2 – 93,5	98,2 – 100,0
Two dose	99,6 %	67,8 %	99,6 %
at 2 and 4 mo	98,1 – 100,0	62,5 – 72,7	98,1 – 100,0

*Blood draw one month after vaccination

**Blood draw immediately prior to booster vaccination

Immunogenicity in Toddlers

In a study investigating the immune response of a single dose of NeisVac-C 100% of the toddlers presented with an rSBA titre of at least 1:8.

Immunogenicity in children aged 3.5-6 years

In a study investigating the immune response of a single dose of NeisVac-C 98.6% of the children presented with an rSBA titre of at least 1:8.

Immunogenicity in adolescents aged 13-17 years and adults

In a study investigating the immune response of a single dose of NeisVac-C 100% of adolescents presented with an rSBA titre of at least 1:8.

In a clinical study in adults aged 18 to 64 years, 95.6% not previously vaccinated and 97.1% with a history of previous vaccination with a plain polysaccharide Men C vaccine had SBA titres of at least 1:8 after a single dose of NeisVac-C.

Post-marketing surveillance following an immunisation campaign in the UK

Estimates of vaccine effectiveness from the UK’s routine immunisation programme (using various quantities of three meningococcal group C conjugate vaccines) covering the period from introduction at the end of 1999 to March 2004 demonstrated the need for a booster dose after completion of the primary series (three doses 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% confidence intervals 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 fall in effectiveness within these age cohorts when comparing time periods less than a year or one year or more since immunisation.

Post-marketing surveillance following immunisation in the Netherlands

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. The catch-up campaign in the Netherlands covered nearly 3 million subjects (94% coverage). 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.

5.2 Pharmacokinetic properties

Pharmacokinetic studies are not required for vaccines.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of pharmacology, pyrogenicity, single and repeated dose toxicity, or toxicity to reproduction and development.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride

Water for injections

6.2 Incompatibilities

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

6.3 Shelf life

42 months

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C). Do not freeze.

Keep the syringe in the outer carton in order to protect from light.

Within the indicated shelf life of 42 months the product may be stored at room temperature (up to +25°C) for a maximum single period of 9 months. During this period, the product may be returned to the refrigerator at 2-8°C. If stored at room temperature (up to +25°C) the starting date and the revised 9 months expiry date should be stated on the product package. The revised expiry date for storage at room temperature must not exceed the expiry date set in accordance with the total shelf life of 42 months.

6.5 Nature and contents of container

NeisVac-C is presented as a 0.5 ml suspension in pre-filled syringe (type I glass) with a cap (bromobutyl rubber) and a plunger stopper (bromobutyl rubber) in packs of 1 or 10 or 20.

Each pre-filled syringe is packed in a blister. The opening in the blister seal is intended and allows for the equilibration of moisture during the recommended warm-up prior to the administration of the vaccine. Open the blister by removing the lid to take out the syringe. Do not press the syringe through the blister.

The pack of 1 may include up to two needles of different sizes. All needles are sterile and for single use only.

The primary packaging is latex-free.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

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

Any unused medicinal product or waste material should be disposed of in accordance with local requirements. It is recommended to use the smaller one (0.50 x 16 mm) of the needles that may be included in the single packs for injection in children and the larger needle (0.60 x 25 mm) for vaccination in adults.

7 MARKETING AUTHORISATION HOLDER

Pfizer Healthcare Ireland
9 Riverwalk
National Digital Park
Citywest Business Campus
Dublin 24

8 MARKETING AUTHORISATION NUMBER

PA0822/183/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 13 July 2001

Date of last renewal: 17 July 2010

10 DATE OF REVISION OF THE TEXT

April 2015