

SUMMARY OF PRODUCT CHARACTERISTICS

NeisVac-C¹

1. NAME OF MEDICINAL PRODUCT

NeisVac-C, 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.....	0.5 mg Al ³⁺

For excipients, see 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

Active immunisation of 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

Posology

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 immunisation

Infants from 2 months of age up to 12 months:

Two doses, each of 0.5 ml, should be given with an interval of at least two months.
(See sections 4.5 and 5.1 regarding co-administration of NeisVac-C with other vaccines)

Children one year of age and older, adolescents and adults: a single 0.5 ml dose.

Booster doses

It is recommended that a booster dose should be given after completion of the primary immunisation series in infants. The timing of this dose should be in accordance with

¹ NeisVac-C is a trademark of Baxter International Inc.

available official recommendations. Information on responses to booster doses and on co-administration with other childhood vaccines is given in sections 5.1 and 4.5, respectively.

The need for booster doses in subjects primed with a single dose (i.e. aged 12 months or more when first immunised) has not yet been established.

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.

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 4.5).

4.3. Contra-indications

Hypersensitivity to any component of the vaccine, 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.

The vaccine should be given with caution to individuals with thrombocytopenia or any coagulation disorder. No data are available on subcutaneous administration of NeisVac-C, therefore the possibility of any toxicity or reduced efficacy is unknown.

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.

In subjects deficient in producing antibody (eg, 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-incident meningitis should therefore be maintained.

Immunisation with 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. Interactions 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)

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 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.

Specific data on concomitant administration of NeisVac-C with Hexavac (DTaP-IPV-HBV-Hib) to infants in a 3-dose primary series indicated that responses to the

hepatitis B component were unsatisfactory. Therefore, concomitant administration with Hexavac is not recommended.

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.

There are no data on concomitant use of NeisVac-C with pneumococcal conjugate vaccine, however, concomitant use should be considered if medically important.

4.6. Pregnancy and Lactation

There are no data on 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.

The risk - benefit relationship should also be examined before making the decision as to whether to immunise during lactation.

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

Adverse Reactions from Clinical Trials

In controlled clinical studies NeisVac-C was often given at the same time as vaccines containing diphtheria and tetanus toxoid (DT), wP, aP, Hib, oral polio virus (OPV), IPV or hepatitis B virus (HBV) in infants, MMR in one-year-olds, DT in children 3.5-6 years, and tetanus and reduced diphtheria toxoid (Td) in 13 – 17 year-olds. NeisVac-C and concomitant injectable vaccines were administered at different sites.

For the most common adverse reactions reported in these studies, see table below.

Frequency of Adverse Reactions	Adverse Reactions
Very common	Injection site reactions: (redness, tenderness/pain, swelling)

(>1:10)	Pain in limb in older children Headache Crying and irritability in infants and toddlers Drowsiness/somnolence/impaired sleeping in infants and toddlers Vomiting/ nausea/ diarrhea in infants Loss of appetite in infants
Common (>1:100 and <1:10)	Fever Loss of appetite in children Vomiting/ nausea/ diarrhea in children Muscle pain in older children and adults Pain in limb in children

Adverse Reactions from Post Marketing Surveillance (for all age groups)

These frequencies are based on spontaneous reporting rates and have been calculated using number of reports and number of doses distributed.

Immune System Disorders:

Very rare (<0.01%): lymphadenopathy, anaphylaxis, hypersensitivity reactions including bronchospasm, facial oedema and angioedema

Nervous System Disorders:

Very rare (<0.01%): 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.

Gastrointestinal Disorders:

Very rare (<0.01%): vomiting, and nausea

Skin and Subcutaneous Tissue Disorders:

Very rare (<0.01%): rash, urticaria, and pruritus

Musculoskeletal, Connective Tissue and Bone Disorders:

Very rare (<0.01%): arthralgia

Renal and Urinary disorders:

Relapse of nephrotic syndrome has been reported in association with Meningococcal group C conjugate vaccines.

Very rarely, petechiae and/or purpura have been reported following immunisation (see also section 4.4).

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

4.9. Overdose

There is no experience with overdose of NeisVac-C vaccine. Overdosing with the vaccine is highly unlikely, because it is administered as a single dose syringe by a health care provider.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic Properties

Pharmacotherapeutic Group: Meningococcal vaccine

ATC code: J07AH

No clinical efficacy studies have been performed.

Serological correlates for protection have not been definitively established for conjugated meningococcal C vaccines; these are under study.

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

In study 99MCIUK (see table below), almost all infants received a diphtheria, tetanus and whole cell pertussis vaccine combined with a Hib conjugate vaccine at the same time as each dose of NeisVac-C (one, two or three doses were given according to randomised treatment group).

- Among infants given a single dose of NeisVac-C at 2 months of age (n=182), 98.4% achieved a SBA titre of at least 1:8 and 95.6% had a titre of at least 1:32 at one month after vaccination.
- Among infants given two doses at 2 and 4 months of age (n=188), all had antibody titres of 1:8 and 99.5% had titres of at least 1:32 at one month after the second dose.
- A challenge dose of unconjugated meningococcal serogroup C polysaccharide (administered as a licensed A/C vaccine at one-fifth of the recommended dose) in the second year of life induced a SBA titre of at least 1:32 in 98% of children who had received either one (n=166) or two doses (n=157) of NeisVac-C in infancy.

In a clinical study in adults aged 18 to 64 years, a single dose of NeisVac-C was administered to 73 adults not previously vaccinated against serogroup C meningococcal infection and 40 that had previously received vaccine containing unconjugated serogroup C meningococcal polysaccharide. Among those with titres determined at one month post-vaccination, 65/68 (97.1%) not previously vaccinated and 34/35 (95.6%) with a history of vaccination had SBA titres of at least 1:8 while 65/68 and 33/35 had titres of at least 1:128. However, the SBA GMTs were 1758 and 662 in respective groups. Therefore, responses to the conjugated polysaccharide in NeisVac-C were lower in adults that had previously been vaccinated with unconjugated polysaccharide although >90% still achieved a SBA titre of 1:128.

Antibody responses (SBA titres against the C11 strain) are summarised in the table below by age group#:

Study	Number of volunteers achieving titre / total number of volunteers	
	titre \geq 1:8*	titre \geq 1:32*
Infants Study 99MCIUK		
1 dose at age 2 months	179/182 (98.4%)	174/182 (95.6%)
2 doses at age 2 and 4 months	188/188 (100%)	187/188 (99.5%)
3 doses at age 2, 3 and 4 months	172/173 (99.4%)	170/172 (98.8%)
Infants Study 97C002		
Booster with NeisVac-C (4th dose)**		24/24 (100%)
Toddlers	72/72 (100%)	70/72 (97.2%)
3.5-6 years	72/73 (98.6%)	72/73 (98.6%)
13-17 years	28/28 (100%)	28/28 (100%)
Adults		
No previous MenC vaccine	65/68 (95.6%)	***
Previous unconjugated MenC	34/35 (97.1%)	***

* Blood was drawn for serology approximately 4 weeks after vaccination.

** The three doses in infancy had been given at 2, 3 and 4 months

*** 95.6% and 94.3% of subjects, respectively, achieved rSBA titres \geq 1:128

except for infants, all age groups received 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 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 (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. Estimates of effectiveness based on a small number of cases to date indicate that there may also be waning protection in children who received a single priming dose as toddlers. Effectiveness in all other age groups (up to 18 years) primed with a single dose has so far remained around 90% or more within and more than one year after vaccination.

5.2. Pharmacokinetic Properties

Pharmacokinetic studies are not required for vaccines.

5.3. Preclinical Safety Data

There are no preclinical data of relevance to the prescriber, which are not already included in other sections.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride, Water for Injections

6.2 Incompatibilities

NeisVac-C must not be mixed with other vaccines in the same syringe.

6.3 Shelf-Life

42 months

6.4. Special precautions for storage

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

Within the indicated shelf-life of 42 months the product may be stored at room temperature (up to +25°C) for a single period, not exceeding 9 months. 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), pack of 1 or 10 or 20. The pack of 1 may include two needles of different sizes. Both needles are sterile and for single use only. The primary packaging is latex-free.

Not all pack sizes may be marketed.

6.6 Instructions for use and handling

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 visually inspected for any foreign particulate matter and/or any variation of physical aspect prior to administration. In the event of either being observed, discard the vaccine. Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER

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