

# DATA SHEET

## MeNZB Suspension for Injection Meningococcal group B Outer Membrane Vesicle (OMV) Vaccine

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### Qualitative and quantitative composition

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1 dose (0.5 ml) contains:

Outer membrane vesicles from *Neisseria meningitidis* group B (strain NZ 98/254)

measured as amount of total protein\* ..... 25 microgram

\* Adsorbed on aluminium hydroxide (1.65 milligram)

For excipients, see List of excipients.

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### Pharmaceutical form

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Suspension for injection.

Off-white, opalescent suspension.

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### Clinical particulars

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#### ***Therapeutic indications***

MeNZB is indicated for primary immunisation against group B meningococci with the P1.7-b,4\* PorA protein ("New Zealand strain"). The population at risk should be vaccinated with MeNZB to prevent serious systemic disease (septicaemia and meningitis) caused by New Zealand strain serogroup B meningococci.

This vaccine is for use in individuals aged 6 weeks or older

\* According to new classification terminology: P1.7-2,4

#### ***Dosage and method of administration***

This vaccine is for use in individuals aged 6 weeks or older

#### **Dosage**

Three doses, each of 0.5 ml, with an interval of 6 weeks between doses.

For infants less than 6 months of age, four doses are recommended. The doses should be administered at 6 weeks, 3 months, 5 months and 10 months of age (with an interval of 6 weeks between the 1<sup>st</sup> and the 2<sup>nd</sup> dose, of 8 weeks between the 2<sup>nd</sup> and the 3<sup>rd</sup> dose and of not less than 5 months between the 3<sup>rd</sup> and the 4<sup>th</sup> dose).

For infants over the age of 6 months, children and adolescents, three doses, each of 0.5 ml, are recommended with an interval of 6 weeks between doses.

## **Method of Administration**

Intramuscular injection.

The vaccine (0.5 ml) is intended for deep intramuscular injection, preferably in the anterolateral thigh in infants/toddlers and in the deltoid region of the non dominant arm in toddlers, older children, adolescents and adults.

The vaccine can be administered concomitantly with routine immunisation DTaP-IPV, Hib - HBV vaccines . Separate injection sites must be used if these vaccines are administered at the same time (See Warning and Precautions).

The vaccine must not be injected intravenously, subcutaneously, or intradermally and must not be mixed with other vaccines in the same syringe.

## **Contraindications**

Persons having shown signs of hypersensitivity to any component of the vaccine or persons having shown signs of hypersensitivity after previous administration of MeNZB.

As with other vaccines, administration of MeNZB should usually be postponed in persons with an acute febrile illness (fever > 38.5 °C).

## **Warning and Precautions**

The vaccine must not be injected intravenously, subcutaneously, or intradermally.

In the event of any foreign particulate matter and/or variation of the normal physical aspect (off-white, opalescent suspension) being observed, the vaccine should not be used.

Separate injection sites must be used if other vaccines are administered at the same time (see Interaction with other medicinal products and other forms of interaction).

MeNZB has not been evaluated in persons with thrombocytopenia or bleeding disorders. For such individuals the risk of haemorrhage following intramuscularly injection must be evaluated against the benefit of vaccination.

Protection against invasive meningococcal diseases caused by any of the other serogroups of meningococcal bacteria has not been proven for MeNZB. The same holds true for *N. meningitidis* serogroup B other than the New Zealand strain.

Therefore it cannot be assumed that MeNZB will protect against meningococcal diseases caused by any of the other types of meningococcal bacteria (A, C, 29-E, H, I, K, L, W-135, X, Y, or Z, including non-typeable). Furthermore, protection should not be assumed against *N. meningitidis* serogroup B other than the New Zealand strain. Complete protection against infection caused by the New Zealand strain cannot be guaranteed.

Before the injection of any vaccine, the person responsible for administration should take all precautions known for the prevention of allergic or any other reactions. As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in the rare case of an anaphylactic event following administration of a vaccine.

Prior to administration of any dose of MeNZB, the patient, parent or guardian should be asked about the personal history, family history, and recent health status of the vaccine recipient, including immunisation history, current health status, and any adverse event after previous immunisations.

In individuals deficient in producing antibodies or taking medication with an immunosuppressive effect, vaccination may not result in an appropriate protective antibody response. While HIV infection is not a contraindication, MeNZB has not been specifically evaluated in the immunocompromised. Individuals with complement deficiencies and

individuals with functional or anatomical asplenia may mount an immune response to MeNZB; however, the degree of protection that would be afforded is unknown.

Any acute infection and febrile illness is reason for delaying the use of MeNZB except when, in the opinion of the physician, withholding the vaccine entails a greater risk. A minor illness with a temperature of  $\leq 38,5$  °C, such as a mild upper respiratory infection, is not usually reason to postpone immunisation.

Patients, parents or guardians should be informed of the immunisation schedule for this vaccine. Precautions such as the use of antipyretic measures following receipt of this vaccine should be relayed to the parent or guardian and the need to report any adverse event stressed.

### **Interaction with other medicinal products and other forms of interaction**

There are no known interactions with any medications.

MeNZB must not be mixed with other vaccines in the same syringe.

Separate injection sites must be used if other vaccines are administered at the same time (see Warnings and Precautions). Concomitant use of MeNZB with other vaccines different from the routine vaccinations (DTaP-IPV, Hib -HBV) should only be considered if medically important and not on a routine basis.

### **Pregnancy and lactation**

#### **Pregnancy**

There are no adequate data from the use of MeNZB in pregnant women.

Animal studies are insufficient with respect to effects on pregnancy, and/or embryonal/foetal development, and/or parturition, and/or postnatal development (see Preclinical Safety Data). The potential risk for humans is unknown.

#### **Lactation**

Information on the safety of the vaccine during lactation is not available.

### **Effects on ability to drive and use machines**

The vaccine is unlikely to produce an effect on the ability to drive or use machines.

Dizziness has been very rarely reported following vaccination. This may temporarily affect the ability to drive or use machines.

### **Adverse effects**

#### **Adverse Reactions from Clinical Studies with MeNZB**

Adverse reactions reported across all age groups are provided below. The age groups are Infants 6-10 weeks old (523 doses), infants/toddlers 6-24 months (1472 doses), children 8-12 years old (1606 doses) and adults >18 years old (103 doses). Note the following descriptions of frequency have been defined as: Very common ( $\geq 10\%$ ); common ( $\geq 1\%$  and  $< 10\%$ ); uncommon ( $\geq 0.1\%$  and  $< 1\%$ ); rare ( $\geq 0.01\%$  and  $< 0.1\%$ ); very rare ( $< 0.01\%$ ). Adverse reactions were collected on the day of vaccination and each day following for up to 7 days. The majority of reactions were self-limiting and resolved within the follow-up period.

In all age groups injection site reactions (including redness, swelling, and induration) were very common. Tenderness/pain was the most common injection site reaction. However, these were not usually clinically significant. Severe injection site reactions persisting for more than 7 day were uncommon.

Crying (infants), irritability, sleepiness, change in eating habits, diarrhoea and vomiting, and fever of at least 38.0 °C (infants, toddlers) were very common after vaccination. Most of these occurred at a similar rate in the control vaccine groups, where studied. An increase of the body temperature in infants 6 hours after vaccination was observed in up to 20 % of all infants

receiving MeNZB in the trials. Most infants had normal body temperature by the second day after vaccination. There have been very rare reports of febrile convulsion following MeNZB vaccination; individuals have rapidly recovered.

In children and adults very commonly reported adverse reactions include headache, malaise, nausea and myalgia.

**Adverse reactions reported across all age groups over all doses given are provided below**

General disorders:

		fever ≥ 38.0°C axillary
Very common	infants	20%
	infants/toddlers	13%
		fever ≥ 38.5°C sublingual
Common	children	3%
	adults	0%

Injection site reactions:

		redness	swelling	induration	tenderness/pain
Very common	infants	9%	4%	10%	47%
	Infants/toddlers	44%,	25%,	51%	56%,
	children	11%	7%	10%	78%
	adults	16%	9%	17%	95%

Additional reactions reported in infants (first year of life) and toddlers (second year of life) over all doses given

General disorders:

		irritability	change in eating habits	impaired sleeping	Unusual Crying
Very common	infants	80%	35%	54%	44%
	Infants/toddlers	45%	21%	18%	1%

Gastrointestinal disorders:

diarrhoea vomiting

Very common	infants	17%	13%
	Infants/toddlers	11%	8%

Additional reactions reported in older children and adults over all doses given

General disorders:

malaise headache

Very common	children	18%	23%
	adults	21%	26%

Musculoskeletal, connective and bone disorders:

myalgia arthralgia

Common	children	9%	6%
Very common	adults	19%	2%

Gastrointestinal disorders:

Nausea

Common	children	9%	
Very common	adults	13%	

*Adverse Reactions from Clinical Studies with the Norwegian parent vaccine, MenBvac, an OMV vaccine manufactured with a strain from a different sero-(sub)type (B:15:P1.7,16)*

For MenBvac further adverse events were reported including anaphylactic reactions, flu-like symptoms, haematuria, Guillain-Barré syndrome, myalgic encephalomyelitis/chronic fatigue syndrome. All these reactions were very rare and occurred in adolescents and/or adults.

**Additional information:**

Although MenBvac is the parent vaccine of MeNZB the above mentioned adverse events of MenBvac may not necessarily be expected to happen with MeNZB.

**Overdose**

Vaccine formulations of MeNZB containing the double amount of the active ingredient (50 microgram per dose) but the same adjuvant content have been administered in clinical trials with similar reactogenicity to the 25 microgram formulations.

**Pharmacological properties**

**Pharmacodynamic properties**

Pharmacotherapeutic group: Meningococcal vaccines, ATC code: J07A H06

**Mechanism of action:**

A vaccination schedule of three (four for infants) doses MeNZB given with an interval of 6 weeks between doses induces a humoral immune response against the New Zealand strain. The degree and quality of the cellular immune response is not yet established. An immune response against common antigens on other *N. meningitidis* serogroup B sero-subtypes may be elicited.

The duration of protection is not yet established.

**Pharmacodynamic effects:**

No specific pharmacodynamic studies have been conducted with MeNZB, in accordance with its status as a vaccine.

**Clinical efficacy:**

Whilst the immunogenicity of the vaccine gives an indication that clinical protection is likely, this is not yet proven. No prospective efficacy trials have been performed with MeNZB.

Standardised serological correlates for protection have not been definitively established for OMV meningococcal B vaccines; these are under study. The serum bactericidal assay (SBA) provides however a good indication of a probable protection. The SBA referenced in the text below used human serum as a source of complement and has been validated.

Data from trials using a vaccination schedule of 3 doses MeNZB given with an interval of 6 weeks demonstrate that 55% of infants (6 weeks), 74% older infants (6 months), 75% toddlers, 76% children, and 93% adults developed a 4-fold rise (compared with pre-vaccination values) in serum bactericidal antibody titres 4-6 weeks after the third dose. The safety and immunogenicity data on a fourth dose administered at least 5 months after the primary immunisation in infant/toddlers (10 months to 3.5 years of age) justifies the administration of a 4<sup>th</sup> dose to infants who received their first dose when aged less than six months of age. In case the epidemiological situation would require this, a fourth dose should be administered to infants between the 10<sup>th</sup> and the 15<sup>th</sup> month of age.

**Pharmacokinetic properties**

No pharmacokinetic studies have been conducted with MeNZB, in accordance with its status as a vaccine.

**Preclinical safety data**

Preclinical data reveal no special hazard for humans based on conventional studies of single and repeated dose toxicity.

***Pharmaceutical particulars*****List of excipients**

Sodium chloride  
Histidine buffer

For adjuvant see Qualitative and quantitative composition.

**Incompatibilities**

This vaccine must not be mixed with other medicinal products.

**Shelf life**

MenNZB has a shelf life of 48 months.

**Special precautions for storage**

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

**Nature and contents of container**

MeNZB is presented as a 0.5 ml suspension for injection in a colourless single dose Type I glass vial closed with bromobutyl rubber stoppers.

MeNZB is supplied in packs containing ten single dose vials.

**Instructions for use, handling and disposal**

The vaccine (0.5 ml) is intended for deep intramuscular injection. Care must be taken to ensure that the vaccine is not injected into a blood vessel. Shake before use.

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

***Further information***

Provisional Consent for the distribution of MeNZB has been granted under Section 23 of the Medicines Act 1981. This consent is valid for 2 years from 8 July 2008. This vaccine is for use in individuals aged 6 weeks or older.

***Medicine Classification***

Prescription Medicine

***Name and Address***

Sponsor in New Zealand:

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***Date of Preparation***

19 June 2009