

MENCEVAX® ACWY PRODUCT INFORMATION

Group A, C, W₁₃₅ and Y polysaccharide meningococcal vaccine

DESCRIPTION

MENCEVAX ACWY is a lyophilized preparation of purified polysaccharides from *Neisseria meningitidis* (meningococcus) of groups A, C, W₁₃₅ and Y.

It is presented as a white pellet in a glass vial together with a separate vial of clear, colourless, sterile saline solvent. When reconstituted with the solvent supplied the vaccine is ready for subcutaneous injection. Each 0.5 mL dose of reconstituted vaccine contains 50 micrograms of each of the polysaccharide of groups A, C, W₁₃₅, and Y.

Other ingredients

The reconstituted vaccine also contains 12.6 mg of sucrose, 4.5 mg of sodium chloride, 0.1mg of trometamol and water for injections to 0.5mL.

The manufacture of this product includes exposure to bovine derived materials. No evidence exists that any case of vCJD (considered to be the human form of bovine spongiform encephalopathy) has resulted from the administration of any vaccine product.

CLINICAL TRIALS

Immunogenicity data

MENCEVAX ACWY induces the production of bactericidal antibodies against meningococci of the serogroups A, C, W₁₃₅ and Y.

The current formulation of MENCEVAX ACWY was shown to be immunologically non-inferior to the previous formulation of the vaccine in terms of SBA titres against serogroups A, C, W and Y in a randomised trial conducted in Lebanon in 322 participants aged 2-30 years. In a randomised grouping, 161 were vaccinated with the current formulation and 161 received the previous formulation of Mencevax ACWY. A 2-fold limit for non-inferiority in terms of SBA GMT was used to conclude on the non-inferiority of the new formulation of *Mencevax ACWY* to the previous formulation. The Upper limit of the 95% CIs for the adjusted ratios of post-vaccination SBA GMTs is shown below for each serogroup : (see Table 1).

Table 1: Adjusted SBA GMT ratios between current and previous* Mencevax ACWY groups at one month post vaccination (ATP cohort for immunogenicity)

Antibody	Group description	N	Adjusted GMT	Group description	N	Adjusted GMT	Adjusted GMT ratio			
							Ratio order	Value	95% CI	
SBA-MenA	Previous	126	9583.0	Current	139	11700.5	Previous/Current	0.82	0.70	0.96
SBA-MenC	Previous	137	1348.1	Current	146	1471.6	Previous/Current	0.92	0.63	1.32
SBA-MenW	Previous	139	1800.5	Current	145	1767.0	Previous/Current	1.02	0.78	1.33
SBA-MenY	Previous	139	2702.2	Current	147	3004.7	Previous/Current	0.90	0.73	1.10

*Previous formulation contained lactose instead of sucrose and trometamol

N = Number of participants with available results

Antibody titres were measured with the serum bactericidal assay (SBA)

GMT=Geometric mean antibody titre

MenA = *Neisseria meningitidis* of serogroup A; MenC = *Neisseria meningitidis* of serogroup C; MenW = *Neisseria meningitidis* of serogroup W; MenY = *Neisseria meningitidis* of serogroup Y

The immunogenicity of the previous formulation of MENCEVAX ACWY was evaluated in five clinical studies conducted in Belgium, Lebanon, Poland, Taiwan (N=369) in participants aged 2-30 years.

Table 2: Immunogenicity results obtained before and one month after vaccination with a previous formulation* of MENCEVAX ACWY (Clinical Studies, N=369)

Participants with:	MenA % (n/N)	MenC % (n/N)	MenW % (n/N)	MenY % (n/N)
SBA titres \geq 1:8				
2-5 years of age				
Pre	88.0% (103/117)	17.3% (23/133)	37.5% (42/112)	74.2% (98/132)
Post	99.3% (134/135)	83.7% (113/135)	95.6% (109/114)	100% (140/140)
\geq 6 years of age				
Pre	99.5% (191/192)	47.0% (93/198)	50.3% (98/195)	82.7% (158/191)
Post	100% (196/196)	99.5% (200/201)	99.5% (201/202)	100% (202/202)
Vaccine response				
2-5 years of age	69.1% (76/110)	79.4% (100/126)	89.3% (100/112)	76.3% (100/131)
\geq 6 years of age	72.2% (135/187)	95.4% (188/197)	92.3% (180/195)	81.2% (155/191)
Seroconversion rate				
2-5 years of age	90.9% (10/11)	78.6% (81/103)	92.9% (65/70)	100% (34/34)
\geq 6 years of age	100% (1/1)	99.0% (103/104)	100% (97/97)	100% (33/33)

*Previous formulation contained lactose instead of sucrose and trometamol

N = Number of participants with available results

n = Number of participants with titre within pre-specified range

Antibody titres were measured with the serum bactericidal assay (SBA). Vaccine response was defined as seroconversion for initially seronegative participants (with SBA titre below 1:8) or as four-fold increase in SBA titre from pre to post vaccination for initially seropositive participants.

MenA = *Neisseria meningitidis* of serogroup A; MenC = *Neisseria meningitidis* of serogroup C; MenW = *Neisseria meningitidis* of serogroup W; MenY = *Neisseria meningitidis* of serogroup Y

Studies conducted among late complement component deficient participants (LCCD) (N=31) and participants after Bone Marrow Transplant (BMT) (N=44) demonstrated that vaccination with Mencevax ACWY elicited a satisfactory immune response.

In LCCD patients (Platonov et al, 2003), the total concentration of antibodies to meningococcal polysaccharides increased significantly 1 month after vaccination and remained elevated for 3 years. Revaccination of LCCD patients 3 years after the first dose restored the total antibody concentration to those observed 1 year after the first vaccination (See table 3).

Table 3: Meningococcal antibody concentrations in late complement component deficient (LCCD) patients before and at different time points after vaccination and revaccination with tetravalent meningococcal capsular polysaccharide vaccine.

	Before vaccination (N=31)	At 13 weeks (N=17)	At 1 year (N=18)	At 3 years after first vaccination, before revaccination (N=16)	At 1 year after revaccination (N=12)
MenA (µg/mL)	5.8 (1.0-124)	26.8 (4.9-963)	31.2 (3.7-185)	11.3 (1.7-79)	32.0 (5.4-65)
MenC (µg/mL)	1.7 (0.14-101)	19.2 (2.2-245)	24.4 (0.2-135)	8.4 (1.4-238)	24.0 (5.6-75)
MenW (µg/mL)	0.9 (0.2-26.0)	16.4 (1.0-99)	17.8 (0.4-105)	8.5 (0.5-133)	8.9 (0.5-57)
MenY (µg/mL)	2.0 (0.3-31.7)	30.7 (3.0-334)	34.5 (0.2-261)	9.4 (1.9-151)	18.7 (5.8-120)

N = Number of sera available

MenA = *Neisseria meningitidis* of serogroup A; MenC = *Neisseria meningitidis* of serogroup C; MenW = *Neisseria meningitidis* of serogroup W; MenY = *Neisseria meningitidis* of serogroup Y

Platonov AE, Vershinina IV et al. Long term effects of patients deficient in a late complement component with a tetravalent meningococcal polysaccharide vaccine. *Vaccine* 2003; 21; 4437-4447.

BMT recipients received Mencevax ACWY either eight or twenty months after BMT (Parkkali et al, 2001). One month after vaccination, the percentage of participants with anti-polysaccharide A concentrations ≥ 2.0 µg/ml were 62% and 84%, and the percentage of participants with anti-polysaccharide C concentrations ≥ 2.0 µg/ml 76% and 84% for the groups of participants receiving the vaccine respectively eight or twenty months after BMT.

Parkkali T, Kaythy H et al. Tetravalent meningococcal polysaccharide vaccination is immunogenic in adult allogenic BMT recipients. *Bone Marrow Transplantation* 2001; 27:79-84.

Efficacy data

In response to a meningococcal disease epidemic in Burkina Faso, a mass vaccination campaign with MENCEVAX ACW was performed in more than 1.68 million children and adults aged from 2 to 29 years. Following this mass vaccination campaign 32 cases of meningitis due to *Neisseria meningitidis* serogroup A and 3 cases of meningitis due to *Neisseria meningitidis* serogroup W₁₃₅ were reported. The corresponding vaccine efficacy against probable/definite *Neisseria meningitidis* serogroup A was

94.0% (95%CI 58.7;99.0) for persons with verified vaccination. The small number of *Neisseria meningitidis* serogroup W135 did not allow estimation of vaccine efficacy against this serogroup.

Persistence of immune response

Literature data supports the persistence of vaccine induced antibody response for at least 3 years.

An ongoing clinical study with the previous formulation* of MENCEVAX ACWY has demonstrated that 100% of participants aged 18-25 years had SBA titres \geq 1:8 against meningococci of the serogroups A, W₁₃₅ and Y and 96% for serogroup C two years after vaccination.

In a study conducted in Ghana with the previous formulation* of MENCEVAX ACWY in 177 participants aged 15-34 years, 100%, 88.4% and 93.5% of participants had SBA titres \geq 1:8 for serogroup A, C and W, respectively at approximately one year after vaccination with MENCEVAX ACWY.

*Previous formulation contained lactose instead of sucrose and trometamol.

In studies conducted among complement-deficient participants, the antibodies persisted for 3 years post vaccination with MENCEVAX ACWY and the revaccination restored antibody concentrations.

INDICATIONS

MENCEVAX ACWY is indicated for active immunisation of adults and children over two years against meningococcal meningitis caused by group A, group C, group W₁₃₅ and group Y meningococci.

The vaccine may be used for :

1. Individuals who are close contacts of patients with disease caused by meningococci of groups A, C, W₁₃₅ and Y.
2. Travellers to countries where the disease is endemic or highly epidemic.
3. Controlling epidemics of infection caused by group A, C, W₁₃₅ and Y meningococci in confined communities.
4. Patients with inherited defects of properdin or complement, or functional or anatomical asplenia.

MENCEVAX ACWY is not recommended for use in infants and children under two years of age as antigenicity of the vaccine is low in this age group and antibodies persist for shorter duration.

CONTRAINDICATIONS

Hypersensitivity to the active substances or to any of the excipients (*see section "DESCRIPTION"*).

Hypersensitivity reaction after previous administration of MENCEVAX ACWY.

PRECAUTIONS

MENCEVAX ACWY is for subcutaneous use only, and should under no circumstances be administered intravascularly or by intradermal injection.

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of anaphylactic reactions following the administration of the vaccine.

Vaccination should be preceded by a review of the medical history (especially with regard to previous vaccination and possible occurrence of undesirable events) and a clinical examination.

As with other vaccines, the administration of MENCEVAX ACWY should be postponed in patients suffering from acute severe febrile illness. However, the presence of a minor infection, such as a cold, should not result in the deferral of vaccination.

MENCEVAX ACWY will only confer protection against *Neisseria meningitidis* serogroups A, C, W₁₃₅ and Y. As for any vaccine, complete protection cannot be guaranteed in every vaccinated individual.

Group C, W₁₃₅ and Y polysaccharides are poorly immunogenic in children less than 24 months of age. Group A polysaccharide induces an antibody response in children from the age of 6 months. However, the response is lower than that observed in older subjects and may be transient.

Group C polysaccharide may induce immunological hyporesponsiveness to further doses of polysaccharide C or to meningococcal group C conjugate vaccine. The clinical relevance of this phenomenon remains unknown.

If administered to patients with impaired immune responses, the vaccine may not induce an effective response.

Immune response to the vaccine may be impaired after acute malaria.

The use of MENCEVAX ACWY may increase the meningococcal carriage rates, especially for meningococcal groups not included in the vaccine.

Interactions

No information is available concerning the effects of drugs, intercurrent illnesses, or other vaccines on the response to the administration of MENCEVAX ACWY.

Different injection sites should be used when concomitant administration with other injectable vaccines can not be avoided.

Use in pregnancy (Category B2)

Adequate human data on use during pregnancy and adequate animal reproduction studies are not available. There is no convincing evidence of risk to the foetus from immunisation of pregnant women using an inactivated bacterial vaccine. However, the vaccine should not be given to pregnant women unless the benefits to the mother clearly outweigh any risk to the foetus.

Use in Lactation

Adequate data on the administration of MENCEVAX ACWY to women who are breast-feeding are not available. However, as with other polysaccharide vaccines, it is not expected for vaccination with MENCEVAX ACWY to harm the mother or the infant. MENCEVAX ACWY should only be administered to women who are breast-feeding when needed and the possible advantages outweigh the possible risks.

Ability to perform tasks that require judgement, motor or cognitive skills

The clinical condition of the patient and the adverse event profile of MENCEVAX ACWY should be borne in mind when considering the patient's ability to perform tasks that require motor or cognitive skills (See ADVERSE EVENTS section below).

ADVERSE REACTIONS

Local and systemic adverse reactions especially febrile reactions may be encountered more frequently in children than in adults.

The safety profile presented below is based on data from clinical studies with a previous formulation of MENCEVAX ACWY where the vaccine was administered to 369 participants. Data generated with the current formulation of MENCEVAX ACWY (N=161) has shown an equivalent safety profile.

Adverse reactions occurring during these studies were mostly reported within 48 hours following vaccination.

Adverse reactions considered as being at least possibly related to vaccination have been categorised by frequency as follows.

Frequencies are reported 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: $< 0.01\%$

Metabolism and nutrition disorders:

Common: appetite lost

Psychiatric disorders:

Very common: irritability

Nervous system disorders:

Very common: drowsiness, headache

Uncommon: dizziness

Very rare: somnolence, neurological reactions

Gastrointestinal disorders:

Common: gastrointestinal symptoms e.g. nausea, vomiting and diarrhoea

Musculoskeletal and connective tissue disorders:

Common: myalgia

Blood and lymphatic system disorders:

Very common: local axillary lymphadenopathy

Respiratory, thoracic and mediastinal disorders:

Uncommon: upper respiratory tract illness

General disorders and administration site conditions:

Very common: erythema, induration, tenderness, pain and redness at the injection site, fatigue, malaise

Common: swelling at the injection site, fever, febrile reactions (>38°C)

In addition, the following adverse reactions have been reported during post-marketing surveillance:

Immune system disorders

Allergic reactions, including anaphylactic and anaphylactoid reactions

Skin and subcutaneous tissue disorders

Urticaria, rash, angioneurotic oedema

Musculoskeletal and connective tissue disorders

Arthralgia, musculoskeletal stiffness

General disorders and administration site conditions

Influenza-like symptoms, chills

DOSAGE AND ADMINISTRATION

MENCEVAX ACWY should be reconstituted only with the saline solvent supplied by adding the entire contents of the supplied vial of solvent to the vaccine vial. The reconstituted vaccine should be inspected for any foreign particulate matter and/or colouration prior to administration. In the event of either being observed, discard the vaccine.

Dosage

The recommended dose for vaccines in all age groups is 0.5mL, administered as a single dose.

Administration

The reconstituted vaccine should be administered subcutaneously with a sterile syringe and needle.

MENCEVAX ACWY should under no circumstances be administered intravenously (see PRECAUTIONS).

Do not mix MENCEVAX ACWY in the same syringe with other medicinal products including other vaccines and drugs.

The NHMRC guideline recommends that a period of 6 months should lapse before administration of a conjugate vaccine after a polysaccharide vaccine. If a conjugate vaccine is given first, a period of at least 2 weeks should lapse before a polysaccharide vaccine is given.

Booster doses

MENCEVAX ACWY should be used in accordance with available official recommendations.

Patients who remain at increased risk of invasive meningococcal disease may be revaccinated at intervals (see persistence of immune response). Intervals should be in accordance with the current Australian NHMRC recommendations for Meningococcal polysaccharide vaccines.

OVERDOSAGE

Cases of overdose (up to 10 times the recommended dose) have been reported during post-marketing surveillance. Adverse events reported following overdose were similar to those reported with normal vaccine administration.

RECOMMENDED STORAGE AND SHIPMENT CONDITIONS

The lyophilized vaccine should be stored in a refrigerator between +2°C and +8°C or in the freezer. The solvent can be stored at ambient temperatures.

MENCEVAX ACWY is stable for at least three years when stored between +2°C and +8°C.

After reconstitution, the vaccine should be injected promptly or kept in a refrigerator. If it is not used within eight hours, it should be discarded because of the risk of contamination.

It is recommended to protect the reconstituted vaccine from direct sunlight.

When supplies of MENCEVAX ACWY are distributed from a central cold-store, it is good practice to arrange transport under refrigerated conditions, particularly in hot climates.

PRESENTATION

Monodose vials supplied with a container of sterile saline solvent for reconstitution of the lyophilized vaccine.

MANUFACTURED BY

GlaxoSmithKline Biologicals

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Issue 9