Mencevax ACWY

MIMS Abbreviated Prescribing Information
Neisseria meningitidis vaccine
GlaxoSmithKline Australia
Section: **10(a)** Vaccines - Immunology
Use in pregnancy: B2
ADRAC
Permitted in sport

Use: Polysaccharide vaccine. Active immunisation against meningococcal meningitis (groups A, C, W_{135}, Y) in adults, children > 2 yrs; close contacts of patients with disease; travellers to endemic, highly epidemic countries; epidemic control in confined communities; properdin, complement inherent defects; functional, anatomical asplenia
Contraindications: Previous hypersensitivity
Precautions: Not for intravascular, intradermal admin; prevaccination medical history, clinical exam; acute severe febrile illness; impaired immunity eg after acute malaria; intercurrent illness (no information); pregnancy, lactation; children < 2 yrs
Adverse Reactions: Appetite lost; irritability; drowsiness; headache; GI upset; myalgia; local axillary lymphadenopathy; inj site reaction; fatigue; malaise; fever; others, see full PI
Interactions: Conjugate vaccine (less than or equal to 2 wks before, less than or equal to 6 mths after); concomitant vaccines (use different inj site); admix with other drugs, vaccines

Mencevax ACWY (Powder for injection) **Rx** (S4) **CMI**
Neisseria meningitidis (meningococcus) groups A 50 mcg, C 50 mcg, W_{135} 50 mcg and Y 50 mcg (purified polysaccharides) per 0.5 mL; sucrose, NaCl; white lyophilised; vial
Dose: Reconstitute with saline solvent. Adults, children > 2 yrs: 0.5 mL SCI as single dose. Revaccinate at intervals recommended by NHMRC for patients who remain at incr risk
Pack 0.5 mL (+ solv) [1] : $44.46

MIMS Full Prescribing Information
MIMS revision date: 01 May 2009
Name of the medicine Each 0.5 mL dose of reconstituted vaccine contains 50 microgram of each of the polysaccharide of groups A, C, W_{135} and Y.
Excipients. Sucrose 12.6 mg, sodium chloride 4.5 mg, trometamol 0.1 mg and water for injections to 0.5 mL.
Description Mencevax ACWY is a lyophilised preparation of purified polysaccharides from *Neisseria meningitidis* (meningococcus) of groups A, C, W_{135} 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. The manufacture of this product includes exposure to bovine derived materials. No evidence exists that any case of variant Creutzfeldt-Jakob disease (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 W_{135} and Y.
The current formulation of Mencevax ACWY was shown to be immunologically noninferior 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 to 30 years. In a randomised grouping, 161 were vaccinated with the current formulation and 161 received the previous formulation of Mencevax ACWY. A twofold limit for noninferiority in terms of SBA GMT was used to conclude on the noninferiority 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).

Mencevax ACWY **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 LL	95% CI UL
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

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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 to 30 years (see Table 2).

Mencevax ACWY **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 ≥ 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)
≥ 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)
≥ 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)
≥ 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).

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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 (mcg/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 (mcg/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 (mcg/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 (mcg/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 mcg/mL were 62% and 84%, and the percentage of participants with anti-polysaccharide C concentrations ≥ 2.0 mcg/mL 76% and 84% for the groups of participants receiving the vaccine respectively eight or twenty months after BMT.

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 W_{135} 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 W_{135} 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 to 25 years had SBA titres ≥ 1:8 against meningococci of the serogroups A, W_{135} 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 to 34 years, 100%, 88.4% and 93.5% of participants had SBA titres ≥ 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 Active immunisation of adults and children over two years against meningococcal meningitis caused by group A, group C, group W_{135} 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, W_{135} and Y.
2. Travellers to countries where the disease is endemic or highly epidemic.
3. Controlling epidemics of infection caused by groups A, C, W_{135} 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 2 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 Composition).

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, W_{135} and Y. As for any vaccine, complete protection cannot be guaranteed in every vaccinated individual.

Group C, W_{135} 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

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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 meningococcal carriage rates, especially for meningococcal groups not included in the vaccine.
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 fetus 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 risks to the fetus.
Use in lactation. Adequate data on the administration of Mencevax ACWY to women who are breastfeeding 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 breastfeeding when needed and the possible advantages outweigh the possible risks.
Effect on ability to drive or operate machinery. 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 Reactions).
Interactions with other medicines 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.
Adverse effects 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: ≥ 10%; common: ≥ 1% and < 10%; uncommon: ≥ 0.1% and < 1%; rare: ≥ 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 postmarketing 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 vaccinees in all age groups is 0.5 mL, 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 ten times the recommended dose) have been reported during postmarketing surveillance. Adverse events reported following overdosage were similar to those reported with normal vaccine administration.
Presentation Monodose vial (white, lyophilised pellet for reconstitution), supplied with container of sterile saline solvent.
Storage The lyophilised vaccine should be stored in a refrigerator at 2 to 8°C or in a freezer. The solvent can be stored at ambient temperatures.

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Mencevax ACWY is stable for at least three years when stored between 2 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.

Poison Schedule S4.

Source Reference Date of TGA approved information: 27/01/2009

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