

DATA SHEET

Name of Medicinal Product

MENCEVAX ACWY

Group A, C, W₁₃₅ and Y polysaccharide meningococcal vaccine

Presentation

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

MENCEVAX ACWY is presented as a white pellet in a glass vial. The sterile diluent is clear and colourless and presented in a glass vial, pre-filled syringe or ampoule.

MENCEVAX ACWY meets the World Health Organisation requirements for biological substances and for meningococcal meningitis vaccines.

Each 0.5ml dose of reconstituted vaccine contains 50 µg of each of the polysaccharide of groups A, C, W₁₃₅ and Y.

Clinical Particulars

Therapeutic 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 also be used for:

- Subjects who are close contacts of patients with disease caused by meningococci of groups A, C, W₁₃₅ and Y.
- Travellers to countries where the disease is epidemic or highly endemic.
- Controlling epidemics of infection caused by group A, C, W₁₃₅, Y meningococci in confined communities.

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.

Posology and method of administration

MENCEVAX ACWY should be reconstituted only with the saline diluent supplied by adding the entire contents of the diluent vial/ampoule/syringe to the vaccine vial. The reconstituted vaccine should be inspected for any foreign particulate matter and/or colouration (other than a possible slight pink cloudiness) prior to administration. In the event of either being observed, discard the vaccine. The vaccine pellet should be completely dissolved in the diluent.

The reconstituted vaccine should be administered subcutaneously with a sterile syringe and needle. For adults and children over 2 years, one dose of vaccine is contained in 0.5ml.

In adults and children over 5 years of age immunity will persist for up to 3 years. Children who were aged under 5 years when first vaccinated should be considered for revaccination after 2-3 years if they remain at high risk (see section "*Pharmacological Properties*").

MENCEVAX ACWY should under no circumstances be administered intravascularly.

Contraindications

MENCEVAX ACWY should not be administered to subjects with known hypersensitivity to any component of the vaccine or to subjects having shown signs of hypersensitivity after previous administration of MENCEVAX ACWY.

Special warnings and special precautions for use

As with other vaccines, the administration of MENCEVAX ACWY should be postponed in subjects 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. If administered to subjects with impaired immune responses, the vaccine may not induce an effective response.

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

Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. It is important that procedures are in place to avoid injury from faints.

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.

Interactions with other medicaments and other forms of interaction

MENCEVAX ACWY can be administered at the same time as other vaccines.

The other injectable vaccines should always be administered at a different injection site.

Pregnancy and lactation

Pregnancy

Adequate human data on use during pregnancy and adequate animal reproduction studies are not available. Mencevax ACWY should be used during pregnancy only when

clearly needed and when the possible advantages outweigh the possible risks for the foetus.

Lactation

Adequate data on the administration of Mencevax ACWY to women who are breast-feeding are not available. However, as with other polysaccharide vaccines, one does not expect vaccination with Mencevax ACWY to harm the mother or the infant. Mencevax ACWY should be administered to women who are breast-feeding when needed and the possible advantages outweigh the possible risks.

Effects on ability to drive and use machines

There have been no studies to investigate the effect of Mencevax ACWY on driving performance or the ability to operate machinery. Further, a detrimental effect on such activities cannot be predicted from the pharmacology of the active substance. Nevertheless, the clinical status 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 judgement, motor or cognitive skills.

Undesirable effects

The safety profile presented below is based on data from clinical studies. 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

Gastrointestinal disorders:

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

Musculoskeletal and connective tissue disorders:

Common: myalgia

General disorders and administration site conditions:

Very common: pain and redness at the injection site, fatigue
Common: swelling at the injection site, fever

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

Overdose

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

Pharmacological Properties

Pharmacodynamic properties

Immunogenicity data

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

The results obtained from clinical studies with a previous formulation* of MENCEVAX ACWY (N = 369) one month after vaccination are summarised in the table below:

Subjects with:	MenA	MenC	MenW	MenY
SBA titres \geq 1:8				
2-5 years of age				
\geq 6 years of age	99.3 %	83.7 %	95.6 %	100 %
	100 %	99.5 %	99.5 %	100 %
Vaccine response				
2-5 years of age	69.1 %	79.4 %	89.3 %	76.3 %
\geq 6 years of age	70.7 %	95.4 %	92.3 %	81.2 %
Seroconversion rate				
2-5 years of age	90.9 %	76.4 %	92.9 %	100 %
\geq 6 years of age	100 %	99.0 %	100 %	100 %

*Previous formulation contained lactose instead of sucrose and trometamol

SBA = Serum bactericidal assay

Vaccine response = seroconversion with SBA titre cut-off of 1:8 for initially seronegative subjects, or a four-fold increase in SBA titres from pre- to post-vaccination for initially seropositive subjects

Data generated with the current formulation of MENCEVAX ACWY (N=161) have shown similar results.

The seroconversion rate of children vaccinated under the age of two years is lower for the serogroup C, W₁₃₅ and Y. However, based on literature data, the seroconversion rate for the serogroup A appears to be acceptable in children from the age of 6 months onwards.

Studies conducted among late complement component deficient subjects (LCCD) (N=31) and subjects after Bone Marrow Transplant (BMT) (N=44) demonstrated that vaccination with MENCEVAX ACWY elicited a satisfactory immune response. In LCCD patients, geometric mean concentrations (GMCs) of 26.8 μ g/ml for MenA, 19.2 μ g/ml for MenC, 16.4 μ g/ml for MenW₁₃₅ and 30.7 μ g/ml for MenY were observed at 13 weeks after vaccination. In BMT patients, 62% to 84% of subjects had anti-polysaccharide A concentrations \geq 2.0 μ g/ml and 76% to 84% of subjects had anti-polysaccharide C concentrations \geq 2.0 μ g/ml one month after vaccination.

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.

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 subjects 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 subjects aged 15-34 years, 100%, 88.4% and 93.5% of subjects 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 subjects, the antibodies persisted for 3 years post vaccination with MENCEVAX ACWY and the revaccination restored antibody concentrations.

Pharmacokinetic properties

Evaluation of pharmacokinetic data is not required for vaccines.

Preclinical safety data

Not applicable.

Pharmaceutical Particulars

Excipients

Powder: sucrose, trometamol

Diluent: sodium chloride, water for injections

Special precautions for storage

The lyophilised vaccine should be stored in a refrigerator between 2°C and 8°C, or in a freezer. The diluent can be stored at ambient temperatures.

After reconstitution, the vaccine should be injected promptly or kept in a refrigerator. If not used within 8 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.

Additional information on stability

Experimental data show that the powder is stable at 37°C for 1 week. However, these data are not recommendations for storage.

Shelf life

The expiry date of the vaccine is indicated on the label and packaging. When stored under prescribed conditions of temperatures between 2°C and 8°C the shelf-life is 3 years.

Medicine Classification

Prescription Medicine.

Package Quantities

Monodose vials. A container of sterile saline diluent is supplied for reconstitution of the lyophilized vaccine.

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