Mencevax™ ACWY

1 - Name of the medicinal product
Mencevax™ ACWY.
2 - Qualitative and Quantitative Composition
Mencevax™ ACWY is a lyophilized preparation of purified polysaccharides from Neisseria meningitidis (meningococcus) of serogroup A, C, W_{135} and Y.
Mencevax™ ACWY meets the World Health Organisation requirements for biological substances and for meningococcal meningitis vaccines.
Each 0.5 ml dose of the reconstituted vaccine contains 50 µg of each of the polysaccharide serogroups A, C, W_{135} and Y.
3 - Pharmaceutical form
Powder and diluent for solution for injection.

4 - Clinical particulars
4.1 Therapeutic indications
Mencevax™ ACWY is indicated for the active immunisation of children from two years of age, adolescents and adults against meningococcal disease caused by meningococci of serogroups A, C, W_{135} and Y.
The vaccine is particularly recommended for subjects at risk, for example those living in or visiting areas where the disease is epidemic or highly endemic.
It is also recommended for subjects living in closed communities and close contacts of patients with disease caused by meningococci of serogroups A, C, W_{135} and Y.
4.2 Posology and method of administration
Posology
The recommended dose of the vaccine contained in 0.5 ml must be administered.
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 5.1 "Pharmacodynamic properties"*).
Method of administration
Mencevax™ ACWY is for **subcutaneous use** only.
4.3 Contra-indications
Hypersensitivity to the active substances or to any of the excipients (*see sections 2 and 6.1*).
Hypersensitivity reaction after previous administration of **Mencevax™ ACWY**.
4.4 Special warnings and special precautions for use
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.
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 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, W_{135} 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.
Mencevax™ ACWY should under no circumstances be administered intravascularly.
4.5 Interaction with other medicaments and other forms of interaction
Mencevax™ ACWY can be administered at the same time as other vaccines. Different injectable vaccines should always be administered at a different injection site.
4.6 Pregnancy and lactation
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.
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.
4.7 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.
4.8 Undesirable effects
Following a widespread use of the vaccine, **Mencevax™ ACWY** is generally well tolerated.
In recent clinical studies, **Mencevax™ ACWY** was administered to 530 subjects.
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%
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

4.9 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.

5 - Pharmacological properties
5.1 Pharmacodynamic properties
Immunogenicity data
Mencevax™ ACWY induces bactericidal antibodies against meningococci of the serogroups A, C, W_{135} and Y.
Clinical studies (N =530) have evaluated one month after vaccination with **Mencevax™ ACWY** the percentage of subjects with bactericidal antibody titres ≥ 1:8, the vaccine response (defined as seroconversion with SBA titre cut-off of 1:8 for initially seronegative subjects or defined as four-fold increase in SBA titres from pre to post-vaccination for initially seropositive subjects) and the seroconversion rate in subjects who were seronegative prior to vaccination. The results obtained in those clinical studies for all serogroups are summarised in the table below:

	MenA	MenC	MenW	MenY
SBA ≥ 1:8				
2-5 years of age	99.4 %	85.8 %	96.6 %	100 %
≥ 6 years of age	100 %	99.7 %	99.7 %	100 %
Vaccine response				
2-5 years of age	74.4 %	81.4 %	90 %	72.4 %
≥ 6 years of age	81.5 %	96.9 %	92.6 %	85.6 %
Seroconversion in S-				
2-5 years of age	93.3 %	83.9 %	95.3 %	100 %
≥ 6 years of age	100 %	99.6 %	100 %	100 %

In studies conducted among Israeli military aged 18 to 55 years, it was demonstrated that **Mencevax™ ACWY** was immunogenic (all subjects had anti-PS concentrations ≥ 2.0µg/ml 2 weeks after vaccination for serogroups A and C).
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, GMCs of 26.8µg/ml for MenA, 19.2 µg/ml for MenC, 16.4 µg/ml for $MenW_{135}$ and 30.7 µg/ml for MenY were observed at 13 weeks after vaccination. In BMT patients, 62% to 84% of subjects had anti-PSA concentrations ≥ 2.0 µg/ml and 76% to 84% of subjects had anti-PSC concentrations ≥ 2.0 µg/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. The vaccine effectiveness against serogroup A and W135 disease was 95.8% (95% CI: 81.8%-99.0%) for persons with reported vaccination.
Persistence of immune response
Literature data supports the persistence of vaccine induced antibody response for at least 3 years.
An ongoing clinical study with **Mencevax™ ACWY** has demonstrated that 100% of subjects aged 18-25 years had bactericidal antibody titers ≥ 1:8 against meningococci for the serogroups A, W_{135} and Y and 96% for serogroup C, two years after vaccination.
In a study conducted in Ghana with **Mencevax™ ACWY,** in 177 subjects aged 15-34 years, 100%, 88.4% and 93.5% of subjects had SBA titres ≥ 1:8 for serogroups A, C and W respectively at approximately one year after vaccination.
In studies conducted among complement-deficient subjects, the antibodies persisted for 3 years post vaccination with **Mencevax™ ACWY** and the revaccination restored antibody concentrations.
5.2 Pharmacokinetic properties
Evaluation of pharmacokinetic is not required for vaccines.
5.3 Preclinical safety data
Non-clinical data reveal no special hazard for humans based on general safety tests performed in animals.
6 - Pharmaceutical particulars
6.1 List of excipients
Vaccine: sucrose, trometamol
Diluent: sodium chloride, water for injections (and phenol for multidose presentations).
6.2 Incompatibilities
In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.
6.3 Shelf life
The expiry date of the vaccine is indicated on the label and on packaging.
When stored under prescribed conditions of temperatures between +2°C and +8°C, the shelf life is three years.
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.
6.4 Special precautions for storage
The lyophilised vaccine should be stored in a refrigerator between +2°C and +8°C. The diluent may also be stored at ambient temperature (25°C).
Experimental data show that the powder is stable when stored at 37°C for 1 week. However, these data are not recommendations for storage.
During transport, recommended conditions of storage must be respected.
6.5 Nature and contents of container
Mencevax™ ACWY is presented as a white powder in a glass vial. The sterile diluent for the monodose presentation is clear and colourless and presented in a glass vial or ampoule.
The sterile diluent for the multidose presentation (which contains phenol) can show a slight cloudiness and/or pink coloration and is presented in a glass vial.
6.6 Instructions for use, handling
The vaccine should be inspected visually for any foreign particulate matter and/or other coloration prior to administration. In the event of either being observed, discard the vaccine.
Mencevax™ ACWY must be reconstituted by adding the entire contents of the supplied container of diluent to the vaccine vial. The vaccine powder should be completely dissolved in the diluent.
Mencevax is a trademark.

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