SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Meningococcal Group A Conjugate Vaccine (Lyophilized) ***MenAfriVac*** 5 micrograms

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose of 0.5 ml reconstituted suspension contains:

Meningococcal A polysaccharide	5 mcg,
Conjugated to Tetanus Toxoid (carrier protein)	5 to 16.5 mcg

3. PHARMACEUTICAL FORM

Lyophilized powder for injection

4. CLINICAL PARTICULARS

4.1. Indications:

Active immunization of young children aged 3 to 24 months for the prevention of invasive meningococcal disease caused by group A N.meningitidis. It does not protect against other forms of invasive disease including purulent meningitis caused by other meningococcus groups (such as Groups B, C, W135, Y, X), by Haemophilus influenzae type b, by Streptococcus pneumoniae, etc. It also does not protect against meningitis caused by other organisms such as viruses, fungi, mycobacteria etc.

4.2. Posology and method of administration:

In children 3 through 9 months of age, MenAfriVac 5 mcg is given as a 2-dose series at least 3 months apart. Children 9 through 24 months of age receive a single dose.

The vaccine is for intramuscular use only. MenAfriVac 5 mcg (Meningococcal A Conjugate vaccine 5 micrograms) should be administered by deep intramuscular injection, preferably into the deltoid muscle or anterolateral aspect of the thigh. The vaccine must not be administered subcutaneously or intravenously, and must not be mixed with other vaccines in the same syringe. Separate injection sites should be used in case of concomitant administration.

4.3. Contraindications:

The vaccine must not be administered to subjects with known hypersensitivity to any component of the product or to subjects having shown hypersensitivity after previous administration of the vaccine. It should not be used in subjects with acute infectious diseases and/or ongoing progressive (acute or chronic) illnesses. Any body temperature ≥ 38ºC or active infection is reason to delay immunization.

4.4. Special warnings and precautions for use:

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available. Since anaphylactic, anaphylactoid or other allergic type reactions are theoretically possible following administration of MenAfriVac 5 mcg, 1:1000 adrenaline and other drugs such as hydrocortisone injection and chlorpheniramine maleate injection should be available for immediate treatment if such reaction occurs. For this reason the vaccinee should remain under medical supervision for 30 minutes after immunization.

Administration of this vaccine does not substitute for routine tetanus vaccination.

No safety or efficacy data are available for the administration of MenAfriVac 5 mcg to individuals living with HIV infection. Practitioners should evaluate the potential risks and benefits of administering the vaccine in these populations, considering the fact that subjects living with HIV infection are at increased risk for meningococcal disease.

Before administration of each dose of MenAfriVac 5 mcg to a child, the child's parent or guardian, should be questioned about possible adverse events after the previous dose or after a previous dose of a TT-containing vaccine.

There is no evidence that MenAfriVac 5 mcg can cause meningococcal meningitis. Clinical alertness to the possibility of co-incidental meningitis should be maintained.

4.5. Interaction with other medicinal products and other forms of interaction:

Drug Interactions:

Administration of the vaccine to immune suppressed persons or persons receiving chronic immunosuppressive therapy, may not elicit an adequate immunologic response. MenAfriVac 5 mcg can be safely and effectively given concomitantly with measles, rubella, yellow fever, diphtheria, tetanus, whole-cell-pertussis, hepatitis B, *Haemophilus influenzae type b* and oral polio vaccines as recommended.

4.6. Pregnancy and lactation:

Not Applicable

4.7. Effects on ability to drive and use machines:

Not Applicable

4.8. Undesirable effects

Safety of MenAfriVac 5 mcg when given concomitantly with EPI vaccines has been evaluated in two clinical trials. MenAfriVac 5 mcg has been found safe. Predominantly mild and transient local reactions at the injection site of MenAfriVac 5 mcg have been reported in less than 9% of infants.

Adverse events (AEs) that were considered related to study vaccine were essentially postimmunization reactions on-going beyond day 4 (mostly induration and gastrointestinal disorders).

No clinically significant differences in the frequency or severity of AEs within 28 days of vaccination were observed among infants receiving MenAfriVac 5 mcg simultaneously with the EPI vaccines compared to EPI vaccines alone, indicating a comparable safety profile. There were no significant increases in systemic reactions due to concomitant administration of MenAfriVac 5 mcg and recommended EPI vaccines compared to the EPI vaccines administered alone. The adverse reactions reported were diarrhoea, injection site tenderness, fever, irritability, vomiting, lethargy, persistent crying, induration, loss of appetite, rash.

Overall rates of reported serious adverse events (SAEs) were similar among study groups at any time during the vaccination series and follow-up observation period. All adverse reactions following immunization were transient and resolved without any sequelae. All other reported adverse events and serious adverse events were unrelated to the MenAfriVac 5 mcg vaccine.

4.9. Overdose:

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties:

Pharmacotherapeutic Group: Meningococcal vaccines, ATC Code: J07AH10

Field efficacy studies have not been performed; rather the effectiveness of the Meningococcal A Conjugate Vaccine 5 µg is based on its ability to induce levels of bactericidal antibodies not inferior to those induced by the licensed meningococcal polysaccharide conjugate vaccine i.e. MenAfriVac 10 µg. A validated serum bactericidal antibody assay using baby rabbit complement (rSBA) was used to measure the functional antibody titer in human sera to Group A Neisseria meningitidis. Immunological non-inferiority was demonstrated in the target population (young children aged 3 to 24 months) based on the following endpoint: seroconversion defined as a ≥ 4-fold increase in MenA rSBA titers. MenA rSBA titers ≥ 1:8 and ≥ 1:128 were assessed as putative correlates for protection and long-term protection to invasive disease caused by Group A Neisseria meningitidis.

Immunogenicity

The primary serological assay used to assess the immunogenicity of the Meningococcal A Conjugate Vaccine 5 µg was rSBA to measure functional antibody activity. This is in line with the WHO recommendation for the evaluation of meningococcal vaccines.
Vaccine response was defined as seroconversion i.e. as a ≥ four-fold increase in rSBA titre from pre to post vaccination.

Two randomized controlled clinical trials were conducted to evaluate reduced antigenic contents of the vaccine compared to the licensed MenAfriVac 10 µg/dose vaccine. The study results demonstrate that the 5 µg dosage is both safe and immunologically non-inferior to MenAfriVac (10 µg) that has shown to be safe and efficacious in the field and confirm that the selected infant dosage, 5 µg, is indeed non-inferior to MenAfriVac (10 µg) and therefore likely to be as effective when used in infants aged 3 to 24 months.

The first study evaluated reduced antigenic contents of Meningococcal A conjugate vaccine-5 µg and 2.5 µg polysaccharide A- conjugated to tetanus toxoid in infants aged 14 weeks at time of the first dose, compared to MenAfriVac (10 µg dose). The second study compared the 5 µg polysaccharide A conjugated to tetanus toxoid in infants aged 9 months to MenAfriVac (10 µg). In both trials, study vaccines were concomitantly given with EPI and rubella vaccines as recommended.

Immunogenicity data in infants aged from 14 weeks (first study) to 9 months (second study) at time of first vaccination indicate that Meningococcal A Conjugate Vaccine 5 µg elicits functional immune responses that are similar to those induced by MenAfriVac (10 µg).

In both studies, non-inferiority of Meningococcal A Conjugate Vaccine 5 µg to MenAfriVac (10 µg) was demonstrated in terms of the primary immunogenicity endpoint for subjects with a seroconversion in MenA rSBA antibody titer.

In the first study, with respect to percentage of subjects with a 4-fold or higher response in MenA rSBA antibody titer with respect to baseline, non-inferiority of Meningococcal A Conjugate Vaccine 5 µg administered in 14 weeks and 9 months of age to MenAfriVac (10µg) administered in 14 weeks and 9 months of age, concomitantly with EPI vaccines, was demonstrated at 28 days after vaccination up to 24 to 27 months after the second dose. The design of the study provided data on the persistence of antibody.

Findings indicate that a schedule consisting of 2 doses of Meningococcal A Conjugate Vaccine 5 µg given at 14 weeks and 9 months of age was highly immunogenic. One month after the second dose, geometric mean titer (GMT) of MenA rSBA was high (5048.6) for Meningococcal A Conjugate Vaccine 5 µg and significantly greater than that achieved by a

single dose of MenAfriVac (10 µg) at 9 months indicating that the first dose of Meningococcal A Conjugate Vaccine 5 µg is effectively priming the immune system. MenA rSBA antibody titers ≥ 1/128 were persisting in 88.1% of subjects in the 5 µg group at the age of 36 months.

In the second study, non-inferiority of 5 µg administered at 9 months of age or administered at 9 months and 15 months of age to MenAfriVac (10 µg) administered in 9 months and 15 months of age, concomitantly with EPI vaccines was established at 28 days after the last vaccine dose. High percentages of subjects developed a 4-fold or higher response in MenA rSBA titer with respect to baseline in all groups.

The Meningococcal A Conjugate Vaccine 5 µg was shown to have an immune response profile over time at least as good as that of MenAfriVac (10 µg), whether administered in a one-or- two-dose schedule. Based on the immune response profile over an extended period of time of the MenAfriVac (10 µg) vaccine when given in a one-dose or two-dose schedule, it is reasonable to predict that the trajectory of immune response of the Meningococcal A Conjugate Vaccine 5 µg will follow a similar trend and that a single dose of this vaccine given from age 9 months onwards will induce sustained antibody levels over time.

It is therefore highly probable that Meningococcal A Conjugate Vaccine 5 µg would be as effective as MenAfriVac (10 µg) to prevent group A meningococcal disease in infants when given as a two dose schedule at the age of 3 months and 9 months, or as one dose schedule given from the age of 9 to 24 months.

5.2. Pharmacokinetic properties:

Evaluation of pharmacokinetics is not required for vaccines.

5.3. Preclinical safety data:

MeriAfriVac has been shown to have no Treatment-related effects in rats and mice following single and repeated (once a week for four weeks) intramuscular administrations at doses equivalent to up to three times the maximal dose intended for use in clinical studies.
In these species, the no-observed-effect-level (NOEL) of Meningococcal Group A conjugate vaccine was found to be greater than 30 µg/animal (i.e. greater than three times the intended human dose).
The local tolerance study carried out in the rabbit and using the intramuscular administration, which is the route, proposed for humans, showed local minor and reversible reactions generally described with adjuvanted/conjugated vaccines.
Preclinical data reveal no special hazard for humans based on general safety tests performed in animals.

6. PHARMACEUTICAL PARTICULARS

6.1. List of Excipients:

Each dose of 0.5 ml reconstituted suspension contains
Mannitol…… 2.85 mg
Sucrose…….. 0.72 mg
Tris (hydroxymethyl) aminomethane (buffer)……...0.06 mg
Aluminium phosphate, Al^{+++} ……..…….…….. not more than 1.25 mg
Thiomersal (preservative)…….0.01%
Sodium chloride…… 0.9%
WFI…….q.s.

6.2. Incompatibilities:

This product must not be mixed with other medicinal products.

6.3. Shelf life:

Shelf life of vaccine: 36 months
Shelf life of Diluent: 54 months
The expiry date of the vaccine and diluent is indicated on the label and packaging.

6.4. Special precautions for storage:

MenAfriVac 5 mcg should be stored and transported between 2-8ºC. Protect from light. The diluent should be stored at below +40ºC, Do not freeze. It is recommended to protect the reconstituted vaccine from direct sunlight. Do not exceed the expiry date stated on the external packaging.

6.5. Nature and contents of the container:

10 dose vaccine vial: 5 ml clear tubular vial USP type I; sealed with rubber stopper and white flip-off seal with copper gold body
10 dose diluent ampoule: 5 ml type I, clear, tubular glass ampoule with one point cut (OPC) mechanism (packed separately)

6.6. Special precautions for disposal:

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

7. MARKETING AUTHORIZATION HOLDER

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8. MARKETING AUTHORIZATION NUMBER(S)

04981/4476/NMR/2017

9. DATE OF FIRST REGISTRATION / RENEWAL OF REGISTRATION CERTIFICATE

06th February 2020 / N.A

10. DATE OF REVISION OF THE TEXT

July 2023