Food and Drugs Authority (FDA)

Public Assessment Report (PAR)

MenFive Vaccine

(Meningococcal (A, C, Y, W, X) Polysaccharide Conjugate Vaccine (Freeze-Dried))

AVCR002/23 (5 doses) & AVCR004/23 (1 dose)

Serum Institute of India Pvt. Ltd, 212/2 Hadapsar, Pune 411028, Maharashtra, India

PART 1: ABSTRACT

MenFive [Meningococcal (A, C, Y, W, X) Polysaccharide Conjugate Vaccine (Freeze-Dried)] (Neisseria meningitidis polysaccharide groups A, C, Y, W and X conjugate vaccine) is a pentavalent meningococcal polysaccharide conjugated vaccine consisting of Neisseria meningitidis capsular polysaccharides A, C, Y, W and X each coupled to a carrier protein. The Neisseria meningitidis serogroups A and X polysaccharides are individually conjugated to Tetanus Toxoid (TT), whereas the C, Y and W polysaccharides are conjugated to Cross Reactive Material 197 (CRM197). MenFive vaccine is manufactured at Serum Institute of India Pvt. Ltd, 212/2 Hadapsar, Pune 411028, Maharashtra, India

The Food and Drugs Authority's Guidelines for the registration of human vaccines defines specific evaluation mechanisms for vaccines with stringent standards for quality, safety, and efficacy.

The marketing authorization of MenFive Vaccine by the FDA is based on reliance pathway in which there was an abridged review of Module 1 to Module 5 of submitted Common Technical Document (CTD) dossier to ascertain the quality, safety, efficacy and sameness of MenFive vaccine prequalified by WHO.

Furthermore, in accordance with the guidelines for safety monitoring of medicinal products in Ghana, a Risk Management Plan (RMP) was submitted and assessed. Applicant satisfactorily outlined their pharmacovigilance plans and safety concerns or risk minimization measures to identify the approach how to identify the risks of the product and which measures will be applied to monitor and minimize such risks in Ghana.

All accepted presentations of MenFive have been shown in Part 2 of this report. The approved Patient Information Leaflet (PIL), Summary of Product characteristics (SmPC) and the approved labelling have been presented in Part 3, Part 4 and Part 5 respectively.
Scientific discussion on the quality, nonclinical and clinical aspects of MenFive vaccine have been presented in Part 6 of this report.

The detailed steps taken to approve MenFive vaccine by the FDA has been presented in Part 7 of this report.

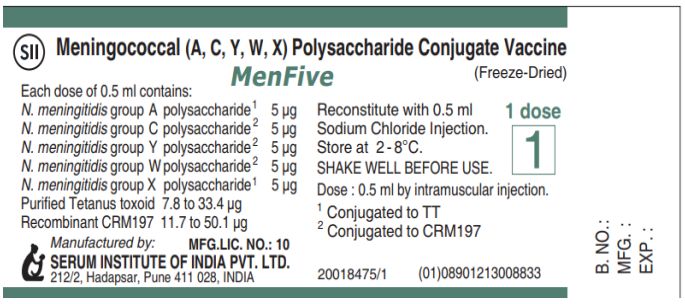
No action or steps have been taken following marketing authorization of MenFive vaccine.

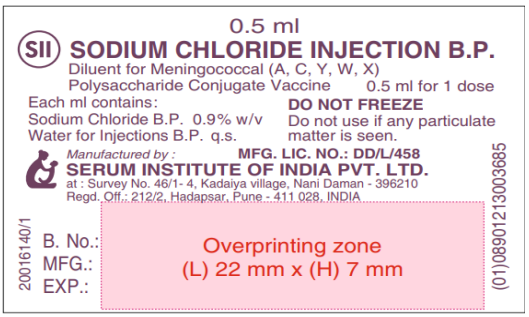
PART 2: ALL ACCEPTED PRESENTATIONS

FDA Registration Number	Brand Name	Strength	Pharmaceutical Form	Route of Administration	Immediate Packaging	Content (concentration)	Pack size
FDA/HVC/241-06012	MenFive 1 Dose (0.5ml)	1*	Freeze-dried powder+ Diluent (.9% Sodium Chloride) for reconstitution	Intramuscular (IM) injection only	Lyophilized Powder: vial (glass) Diluent: Ampoule	Lyopholized powder: 1* Diluent:0.5ml	Box of 50 vials ((1 dose, 5 dose) Box of 50 ampoule (Diluent for 1 dose & 5 dose)
FDA/HVC/241-06013	MenFive 5 Dose (2.5ml)					Lyophilized powder: 1* Diluent:2.5ml	

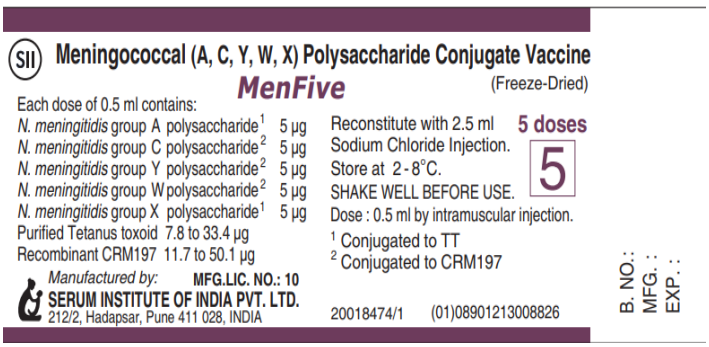
1*=Each (0.5 mL) after reconstitution contains
N. meningitidis group A polysaccharide Conjugated to TT……. 5 µg
N. meningitidis group C polysaccharide Conjugated to CRM197…. 5 µg
N. meningitidis group Y polysaccharide Conjugated to CRM197…. 5 µg
N. meningitidis group W polysaccharide Conjugated to CRM197… 5 µg
N. meningitidis group X polysaccharide Conjugated to TT……... 5 µg
Purified Tetanus Toxoid ……7.8 to 33.4 µg
Recombinant CRM197 ……11.7 to 50.1 µg

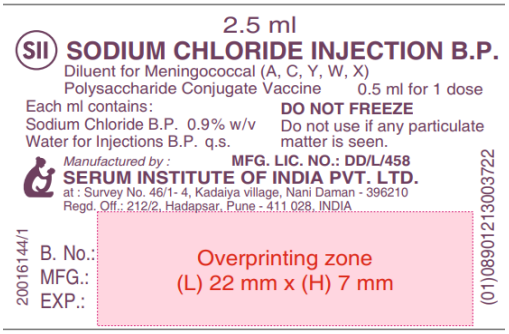
MenFive 1 Dose with diluent





MenFive 5 Dose with diluent





PART 3 : PATIENT INFORMATION LEAFLET

Refer to Part 4 for the Summary of Product Characteristics (SmPC) which suffices in the case of vaccines.

PART 4 : SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

Refer to the FDA website below for the SmPC
www.fdaghana.gov.gh/img/smpc/SmPC%20for%20Menfive%20Vaccine.pdf

PART 5: LABELLING

Primary package label

- Vial label of Meningococcal (A, C, Y, W, X) Polysaccharide Conjugate Vaccine 1 Dose
- Vial label of Meningococcal (A, C, Y, W, X) Polysaccharide Conjugate Vaccine 5 Dose
- Ampoule Label for Diluent for Meningococcal (A, C, Y, W, X) Polysaccharide Conjugate Vaccine 0.5 ml for 1 Dose
- Ampoule Label for Diluent for Meningococcal (A, C, Y, W, X) Polysaccharide Conjugate Vaccine 2.5 ml for 5 Dose

Secondary packaged label

- Box of 50 vials
    - Sticker for box of 50 vials (1 dose, 5 dose)
- Box of 50 ampoule
    - Sticker for box of 50 ampoule (Diluent for 1 dose & 5 dose)

PART 6: SCIENTIFIC DISCUSSION

6.0 SCIENTIFIC DISCUSSION

6.1. About the Product: General information:

- **Name of vaccine:** MenFive (Meningococcal (A, C, Y, W, X) Polysaccharide Conjugate Vaccine (Freeze-Dried))
- **Therapeutic indication**: MenFive is indicated for active immunization of individuals aged 1-85 years against invasive meningococcal disease caused by Neisseria meningitidis serogroups A, C, Y, W, and X.
- **Manufacturer**: Serum Institute of India Pvt. Ltd, 212/2 Hadapsar, Pune 411028, Maharashtra, India
- **Local agent**: M&G Pharmaceuticals Limited, P.O. Box 1681, Accra-Ghana
- **Pharmaceutical form:** Freeze-dried (powder) formulated vaccine available in two presentations viz. 5-dose vial and single-dose vial. The freeze-dried vaccine is to be reconstituted with provided diluent i.e. 0.9% sodium chloride prior to the administration.
- **Storage:** Store in a refrigerator (+2ºC to +8ºC). Do not freeze. Protect from light. Opened multidose vial (After first use): Once opened, multi-dose vials should be used as soon as practically possible and within 6 hours when kept between +2ºC and +8ºC. All opened multidose vials of MenFive should be discarded at the end of immunization session or within six hours, whichever comes first
- **Shelf:** 36 months
- **Product presentation:** MenFive [Meningococcal (A, C, Y, W, X) Polysaccharide Conjugate Vaccine (Freeze Dried)] Drug Product is filled in USP type I glass vial and closed with bromobutyl rubber stopper followed by capping with aluminium flip-off cap.

6.2 Quality Aspect

6.2.1 Drug Substance (DS)

Manufacturer(s): The bulk drug substance is manufactured, tested and released by Serum Institute of India Private Limited (SIIPL) 212/2 Hadapsar, Pune 411028, Maharashtra, India.

M**anufacturing process**: The manufacturing of the Conjugate Bulk Drug Substances used in the Drug product Meningococcal (A, C, Y, W, X) Polysaccharide Conjugate Vaccine (Freeze Dried) i.e MenFive Vaccine (NmCV-5) consists of the following stages - Fermentation, Polysaccharide Purification, Conjugation and Conjugate Purification.

Stability:

Based upon the results of the stability study, the Conjugate Bulk Drug Substance are stable as below;

- up to 36 months when stored in Ultra-low density polyethylene Hyclone (media bag) at ≤ -20℃ or.
- in Ultra-low density polyethylene Hyclone (media bag) for 18 months at ≤ -20℃.

Also, available stability data acquired under real time storage condition (2℃ to 8℃), concluded that the Recombinant Concentrate Bulk is stable for up to 36 months. Hence assigned shelf life and retest period is 36 months.

Further, based upon the results of the stability study, Purified Tetanus Toxoid (GFC) Carrier Protein can be stored in sterile glass bottle for 12 months at +2℃ to +8℃.

6.2.2 Drug Product (DP)

Manufacturer : The drug product is manufactured, tested and released by Serum Institute of India Private Limited (SIIPL) 212/2 Hadapsar, Pune 411028, Maharashtra, India.

Manufacturing Process: The manufacturing process consist of the following steps using product specific batch records and process controls for each operation:

- Formulation
- Drug product preparation steps
    - Preparation of stabilizers and reagents
    - Primary Packaging Material and Process Equipment Preparation and Processing
- Blending and filtration of the NmCV- A, C, Y, W and X conjugates with appropriate excipient concentrations
- Filling and partial stoppering
- Lyophilization and full stoppering
- Sealing of vials (capping)
- Physical inspection
- Labelling and Packaging
- Storage/dispatch

Stability: On the basis of available real time (long term) stability data of 42 months for six batches manufactured for Phase I and Phase II clinical trial and 42 months real time stability data of six batches manufactured for Phase III clinical trial (Phase 3 Africa and India Phase 2/3 Lot to lot consistency) along with Accelerated stability data of ten batches and High accelerated (Stressed) stability data of six batches indicating that Meningococcal A, C, Y, W, X Polysaccharide Conjugate Vaccine-Freeze dried (MenFive) is stable found within specification for 36 months at 2-8°C.

6.2.3 Nonclinical Aspect

6.2.3.1 Pharmacology

The following primary pharmacodynamic nonclinical studies were conducted and submitted by Marketing Authorization Holder for which data submitted for these studies are considered satisfactory.

- A 5-week subcutaneous dose-ranging immunogenicity study of monovalent meningococcal serogroup X polysaccharide conjugate (Men X-TT) with and without aluminum phosphate adjuvant in mice.

- A 7-week subcutaneous immunogenicity study of the Men X-TT component in the NmCV-5 presentation with and without aluminum phosphate adjuvant in mice.

- A 5-week intramuscular immunogenicity study of candidate SIIPL NmCV-5 vaccine formulations in comparison to commercial vaccine in rabbits.

- A 5-week intramuscular dose-ranging immunogenicity study of pentavalent SIIPL NmCV-5 vaccine (tox formulation) with and without aluminum phosphate adjuvant in rabbits.

- A 5-week intramuscular immunogenicity study of the Men A, C, Y, W and X components in the NmCV-5 presentation with and without aluminum phosphate adjuvant in rats.

6.2.3.2 Toxicology studies

The following primary toxicological studies were conducted and submitted by Marketing Authorization Holder for which data submitted for these studies are considered satisfactory.

- A 7-week intramuscular toxicity study of [pentavalent] meningococcal (A, C, Y, W, X) polysaccharide conjugate vaccine (freeze-dried) in New Zealand White rabbits with a 6-week recovery.

- An intramuscular combined development and pre- and postnatal reproductive toxicology study of meningococcal (A, C, Y, W, X) polysaccharide conjugate vaccine, NmCV-5, in Sprague-Dawley rats.

- Single dose oral gavage acute toxicity study of 4 pyrrolidinopyridine in CD® rats followed by a 14-day observation period.

- Single dose intramuscular injection acute toxicology study of 4-pyrrolidinopyridine in CD® rats followed by a 14-day observation period.

- A skin sensitization study (maximization method) of 4 pyrrolidinopyridine in guinea pigs

- Bacterial reverse mutation assay of 4 pyrrolidinopyridine

6.2.4 Clinical Aspects

The Marketing Authorization Holder claimed that the clinical studies were performed in accordance with Good Clinical Practice and all applicable regulatory requirements, including, where applicable, the Declaration of Helsinki. Applicants provided statements that studies were performed in compliance with Good Clinical Practice including the archiving of essential documents.

The following clinical studies were conducted and submitted by Marketing Authorization Holder for which data submitted for these studies are considered satisfactory for clinical safety and efficacy of MenFive vaccine.

- Study Title: A Phase 1, double blind, randomized, controlled study to evaluate the safety and immunogenicity of a new Meningococcal Conjugate Vaccine containing serogroups A, C, Y, W and X in healthy adults.
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- Study Title: A Phase 2, Observer-blind, Randomized, Controlled Study to Evaluate the Safety and Immunogenicity of Two Formulations of Investigational Meningococcal Groups ACYWX Conjugate Vaccine, Administered to Healthy Malian Children 12-16 Months of Age.

- Study Title: A Phase 3, observer-blind, randomized, active controlled trial to assess the safety of an investigational meningococcal serogroups ACYWX conjugate vaccine (NmCV-5) and compare its Immunogenicity to a Licensed Meningococcal Serogroups ACYW Conjugate Vaccine (Menactra®), in Healthy Subjects 2 to 29 Years of Age.

- Phase 2/3 Study: Study Title: A Phase 2/3, Randomized, Observer-blind, Controlled, Multi-Center Study TO Evaluate the Lot-to-Lot Consistency of SIIPL Meningococcal ACYWX Conjugate Vaccine (NmCV-5) and to Compare its Safety and Immunogenicity with that of Licensed Meningococcal ACYW Vaccine Menactra® in Healthy Individuals 18-85 Years of Age.

PART 7: STEPS TAKEN FOR REGISTRATION

7.0 BACKGROUND INFORMATION ON THE PROCEDURE

7.1 Submission of the Dossier

The local agent – M&G Pharmaceuticals – representing Serum Institute of India Pvt. Ltd, 212/2 Hadapsar, Pune 411028, Maharashtra, India, submitted application to the Food and Drugs Authority (FDA) for the registration of MenFive **(**Meningococcal (A, C, Y, W, X) Polysaccharide Conjugate Vaccine (Freeze-Dried) 1 & 5 doses) vaccine.

The following are steps taken for the registration of MenFive vaccine.

Application receipt Date	8th March, 2023
Acknowledgement of Application	25th April 2023
Date of Assessment	30th April 2024-10th May 2024
Product Registration Meeting	24th May, 2024
Date of Conditional Approval	13th June 2024

7.2 Legal basis

The legal basis for the receipt, evaluation, and registration of product is provided below:

- Section 118 (1) of the Public Health Act, 2012, Act 851
- FDA Reliance Guideline on Regulatory Decision-Making (FDA/GEN/GDL - 04/02)
- Guidelines for registration of human vaccines (FDA/VBP/GDL-05/03)
- SOP for evaluation and registration of a Biological Product application (FDA/VBP/SOP -01).
- SOP for good review practices - Biological Product dossier evaluation (FDA/VBP/SOP -05)

This application was reviewed via the FDA Reliance registration pathway

PART 8: STEPS TAKEN FOLLOWING REGISTRATION

No action or steps have been taken following marketing authorization of MenFive vaccine.