Summary of Product Characteristics for Pharmaceutical Products

1 NAME OF THE MEDICINAL PRODUCT

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

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose (0.5 mL) contains:
5 µg of each Meningococcal A, C, Y, W, and X polysaccharide individually conjugated to a carrier protein. The serogroup A and X polysaccharides are conjugated to purified tetanus toxoid (TT) and the serogroup C, W, and Y polysaccharides are conjugated to recombinant CRM197 (cross-reactive material 197, a nontoxic mutant of diphtheria toxin) protein.

Name of Ingredients	**Quantity per dose (0.5 mL) after reconstitution**
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

Excipient with known effect;
Sucrose

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

MenFive is a freeze-dried 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.

5-dose vial:
For the preparation of MenFive, the 5-dose vaccine vial is reconstituted with 2.5 mL of provided diluent i.e. 0.9% sodium chloride.
Single-dose vial:
For the preparation of the of MenFive, the single-dose vaccine vial is reconstituted with 0.5 mL of provided diluent i.e. 0.9% sodium chloride.

Neither the vaccine nor the diluent contains any preservative.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

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.

4.2 Posology and method of administration

Posology
MenFive vaccination course consists of a single dose of 0.5 mL.

Method of administration
MenFive is for intramuscular (IM) injection only, preferably in the deltoid muscle. In children below 5 years of age, the anterolateral aspect of the thigh may be used as alternate site if injection in the deltoid muscle is not feasible. For instructions on administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and special precautions for use

Hypersensitivity including anaphylaxis

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available. Anaphylactic, anaphylactoid or other allergic type reactions are theoretically possible following administration of MenFive.

Concurrent illness

As with other vaccines, administration of MenFive should be postponed in individuals suffering from an acute febrile illness. Any body temperature ≥ 38°C or active infection is reason to delay immunization.

Risk of bleeding with intramuscular administration

As with other intramuscular injections, MenFive should be given with caution to individuals with thrombocytopenia, any coagulation disorder or to persons on anticoagulation therapy, because bleeding or bruising may occur following an intramuscular administration in these individuals.

Immunocompromised individuals

No safety or efficacy data are available for the administration of MenFive 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. It is not known whether individuals with impaired immune responsiveness, including individuals receiving immunosuppressant therapy, will elicit the same response as immunocompetent individuals to the vaccine regimen.

Syncope

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

Duration of protection

The duration of protection has not yet been established.

Protection against meningococcal disease

As with any vaccine, vaccination with MenFive may not protect all vaccine recipients (See section 5.1). MenFive will only confer protection from meningitis

caused by *Neisseria meningitidis* serogroups A, C, W, Y and X. MenFive will not protect from meningitis caused by any other *Neisseria meningitidis* serogroups, other bacteria, viruses, fungi, mycobacteria etc.

Effect of MenFive on anti-tetanus and anti-diphtheria antibody concentrations
Although an increase of the anti-tetanus toxoid and anti-diphtheria antibody concentrations were observed following vaccination with MenFive, it does not substitute for routine tetanus and diphtheria vaccination.

4.5 Interaction with other medicinal products and other forms of interaction

The safety and immunogenicity of co-administration of MenFive with other vaccines have not been evaluated.

4.6 Fertility, pregnancy and lactation

Fertility
Animal studies do not indicate direct or indirect harmful effects with respect to female fertility.

Pregnancy
MenFive has not been evaluated in pregnant women.
Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/fetal development, parturition or post-natal development (See section 5.3).
Administration of MenFive in pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and fetus.

Breastfeeding
It is unknown whether MenFive is excreted in human milk.

4.7 Effects on ability to drive and use machines

MenFive is unlikely to affect the ability to drive and to use machines.

4.8 Undesirable effects

Summary of the safety profile:
The overall safety of MenFive is based on an analysis of data from four clinical trials (ACYWX01, ACYWX-02, ACYWX-03 and ACYWX-04) conducted in the US, Mali, The Gambia and India.

Table 1: Overview of the clinical studies

Study identification	Study country	Study Design	Population (age) Schedule of vaccination	Study groups	Number of participants
ACYWX-01	United States	Randomized, Single Center, Three-Arm, Active Controlled, Observer-Blind Study	Adults (18-45 years inclusive) Schedule of vaccination: 1 dose on Day 0	Adjuvanted MenFive	20
				Non-adjuvanted MenFive*	20
				MenACWY-D	20
ACYWX-02	Mali	Randomized, Single Center, Three-Arm, Active Controlled, Observer-Blind Study	Children (12-16 months inclusive) Schedule of vaccination: 2 doses on Day 0 and Day 84	Non-adjuvanted MenFive	149
				Adjuvanted MenFive	150
				MenACWY-D	76
ACYWX-03	Mali and The Gambia	Randomized, Multi-Center, Two-Arm, Active-Controlled, Observer-Blind Study	Adults (18-29 years inclusive)	MenFive	400
				MenACWY-D	200
			Adolescents (11-17 years inclusive)	MenFive	400
				MenACWY-D	200
			Children (2-10 years inclusive)	MenFive	400
				MenACWY-D	200
			Schedule of vaccination: 1 dose on Day 0		
ACYWX-04	India	Randomized, Multi-Center, Two-Arm, Active-Controlled, Observer-Blind Study	Adults (18-85 years inclusive) Schedule of vaccination: 1 dose on Day 0	MenFive	1233
				MenACWY-D	407

* As there were no significant differences in the reactogenicity and safety profile of the 2 formulations of MenFive (adjuvanted and non-adjuvanted), the data from the adjuvanted formulation are considered as supportive with respect to the reactogenicity and safety profile of the MenFive.

Demographic characteristics were generally similar among participants who received MenFive and those who received control vaccine.

The total number of doses of MenFive administered to participants from 1 to 85 years of age is 3061 (of which 2746 were the non-adjuvanted formulation).

Adverse drug reactions

Adverse drug reactions (ADRs) are organised by MedDRA System Organ Class (SOC). Within each SOC, preferred terms are arranged by decreasing frequency and then by decreasing seriousness. Frequencies of occurrence of adverse reactions are defined as: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1000); very rare (< 1/10,000) and not known (cannot be estimated from available data).

Table 2: Adverse drug reactions

MedDRA SOC	**Frequency**	**Adverse reactions**
Nervous system disorders	Very common	Headache#
	Uncommon	Somnolence*, irritability*
Gastrointestinal disorders	Common	Diarrhea
	Uncommon	Vomiting
Metabolism and nutrition disorders	Common	Anorexia
Musculoskeletal and connective tissue disorders	Common	Myalgia#, arthralgia#
General disorders and administration site conditions	Very common	Injection site pain/tenderness
	Common	Injection site swelling/induration, Pyrexia, fatigue#
	Uncommon	Injection site erythema

*In children below 6 years of age #In participants ≥6 years of age

4.9 Overdose

No case of overdose is reported.

There is no specific treatment for an overdose with MenFive. In the event of an overdose, the individual should be monitored and provided with supportive treatment as per the medical judgement of the physician.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vaccines, Bacterial vaccines, Meningococcal vaccines

ATC code: J07AH

Mechanism of action

Anti-capsular meningococcal antibodies protect against meningococcal disease via complement mediated bactericidal activity. MenFive induces the production of bactericidal antibodies against capsular polysaccharides of *Neisseria meningitidis* serogroups A, C, W, Y, and X when measured by rabbit Serum Bactericidal Assay (rSBA).

Immunogenicity data from the clinical studies:

Immunogenicity data from 4 clinical studies (study design overview presented in Table 1) is summarized below. The functional measure of immunogenicity used in all these studies was a rSBA that measures the ability of antibodies, in concert with rabbit complement, to kill meningococci. Seroresponse was defined as a post-immunization rSBA titer ≥32 for participants with preimmunization rSBA titer < 8, or a ≥ 4-fold increase over baseline for participants with preimmunization rSBA titer ≥ 8.

Study ACYWX-01 (Adults: 18-45 years age)

The seroresponse rate against serogroups A, C, W and Y was high (≥70%) in all treatment groups, while for serogroup X, seroresponse was observed in 95.0% of participants in the adjuvanted

MenFive group, 85.0% in the non-adjuvanted MenFive group, and 5.0% in the licensed MenACWYD group (Table 3).

Table 3: Seroresponse rates against serogroups A, C, Y, W and X, 28 days after vaccination - Per protocol population (Study ACYWX-01)

Serogroup	Non-adjuvanted MenFive (N=20) n (%) (95% CI)	Adjuvanted MenFive (N=20) n (%) (95% CI)	MenACWY-D (N=20) n (%) (95% CI)
A	14 (70.0) (45.7 - 88.1)	17 (85.0) (62.1 - 96.8)	16 (80.0) (56.3 - 94.3)
C	20 (100.0) (83.2 - 100.0)	19 (95.0) (75.1 - 99.9)	17 (85.0) (62.1 - 96.8)
Y	19 (95.0) (75.1 - 99.9)	19 (95.0) (75.1 - 99.9)	15 (75.0) (50.9 - 91.3)
W	19 (95.0) (75.1 - 99.9)	20 (100.0) (83.2 - 100.0)	16 (80.0) (56.3 - 94.3)
X	17 (85.0) (62.1 - 96.8)	19 (95.0) (75.1 - 99.9)	1 (5.0) (0.1 - 24.9)

Fisher's exact 95% CIs.
For percentage calculations, the denominator is the number of participants with nonmissing values at baseline and postvaccination visits.

Although some differences across treatment groups were noted for baseline titers, rSBA geometric mean titers (GMT) against serogroups A, C, W and Y increased in all treatment groups 28 days after vaccination i.e. Day 29. On Day 29, rSBA GMTs tended to be higher in the adjuvanted and nonadjuvanted MenFive groups compared to the MenACWY-D group (Table 4). For serogroup X, an increase in rSBA GMTs was observed in the adjuvanted and non-adjuvanted MenFive groups.

Table 4: rSBA Geometric Mean Titers per Serogroup - Per-Protocol Population (Study ACYWX-01)

Serogroup	Non-adjuvanted MenFive (N=20) GMT (95% CI)	Adjuvanted MenFive (N=20) GMT (95% CI)	MenACWY-D (N=20) GMT (95% CI)
Baseline			
A	350 (119, 1025)	187 (49.6, 708)	33.1 (8.42, 130)

C	4.29 (2.01, 9.15)	9.85 (3.77, 25.7)	5.66 (2.15, 14.9)
Y	24.3 (6.16, 95.4)	10.2 (3.03, 34.4)	53.8 (14.2, 204)
W	26.9 (6.19, 117)	8.00 (2.44, 26.2)	13.9 (4.16, 46.6)
X	5.28 (1.89, 14.8)	6.28 (2.44, 16.1)	3.36 (1.76, 6.43)
28 days after vaccination			
	5595 (3324, 9418)		
A		6889 (3767, 12596)	3214 (1978, 5222)
C	6208 (3579, 10771)	4096 (1720, 9756	388 (139, 1085)
Y	9410 (4935, 17942)	4545 (1700, 12149)	2353 (1302, 4251)
W	11191 (6720, 18635)	8192 (3439, 19513)	1261 (388, 4091)
X	1607 (892, 2895)	1351 (577, 3165)	3.14 (1.73, 5.71)

The percentage of participants with rSBA titers ≥128 on Day 29: it ranged between 95.0% and 100% in both MenFive groups for all five serogroups while it ranged between 90.0% and 100% in MenACWY-D group for serogroups A, C, Y, and W and 10% for serogroup X.

Study ACYWX-02 (Children: 12-16 months' age)

In this study, participants were assigned in a 2:2:1 ratio to receive nonadjuvanted MenFive, alumadjuvanted MenFive, or the licensed quadrivalent vaccine MenACWY-D, administered intramuscularly in two doses 12 weeks apart i.e. on day 0 and 84. Immunogenicity was assessed on days 0, 28, 84, and 112.

At 28 days after the first dose of vaccine, seroresponse was seen in >97% of the participants in each MenFive group for all five serogroups, whereas in the MenACWY-D group it was observed in at least 90% of the participants only for serogroups A and W and was observed in 69.4% of the participants for serogroup C. At the day 112 visit, which was scheduled to be 28 days after the second dose of vaccine, seroresponse was seen in >98% of the participants in all three groups for all the serogroups included in the respective vaccines (Table 5).

Table 5: Seroresponse rates against serogroups A, C, Y, W and X, 28 days after each injection

(Per Protocol population) – Study ACYWX-02

Serogroup	**Non-adjuvanted MenFive (N=144) n (%) (95% CI)**	**Adjuvanted MenFive (N=144) n (%) (95% CI)**	**MenACWY-D (N=72) n (%) (95% CI)**

Day 28			
A	143 (99.3) (96.19, 99.98)	144 (100.0) (97.47,100.00)	70 (97.2) (90.32, 99.66)
C	141 (98.6) (95.04, 99.83)	141 (97.9) (94.03, 99.57)	50 (69.4) (57.47, 79.76)
Y	140 (97.2) (93.04, 99.24)	142 (98.6) (95.07, 99.83)	63 (87.5) (77.59, 94.12)
W	140 (97.9) (93.99, 99.57)	140 (97.9) (93.99, 99.57)	65 (90.3) (80.99, 96.00)
X	144 (100.0) (97.47,100.00)	142 (98.6) (95.07, 99.83)	12 (16.7) (8.92, 27.30)
Day 112			
A	143 (99.3) (96.19, 99.98)	144 (100.0) (97.47, 100.00)	71 (98.6) (92.50, 99.96)
C	142 (99.3) (96.17, 99.98)	144 (100.0) (97.47, 100.00)	72 (100.0) (95.01, 100.00)
Y	144 (100.0) (97.47, 100.00)	142 (98.6) (95.07, 99.83)	71 (98.6) (92.50, 99.96)
W	142 (99.3) (96.17, 99.98)	143 (100.0) (97.45, 100.00)	71 (98.6) (92.50, 99.96)
X	143 (99.3) (96.19, 99.98)	143 (99.3) (96.19, 99.98)	19 (26.4) (16.70, 38.10)

CIs were two-sided 95% Clopper-Pearson CIs.

For percentage calculations, the denominator is the number of participants with nonmissing values at baseline and postvaccination visits.

The rSBA GMTs were notably higher in the non-adjuvanted MenFive and adjuvanted MenFive groups compared to the MenACWY-D group for all serogroups, at all timepoints after vaccination (Table 6).

Table 6: rSBA Geometric Mean Titers per Serogroup before and 28 days after each injection (Per Protocol Population) – Study ACYWX-02

Serogroup	**Non-adjuvanted MenFive (N=144) GMT (95% CI)**	**Adjuvanted MenFive (N=144) GMT (95% CI)**	**MenACWY-D (N=72) GMT (95% CI)**
Day 0 A	3.8 (2.81,5.18)	4.3 (3.08,5.89)	4.4 (2.74,6.95)
C	2.2 (1.97,2.37)	2.0 (NA,NA)*	2.0 (NA,NA)*
Y	3.6 (2.74,4.64)	4.1 (3.08,5.55)	3.9 (2.63,5.86)
W	2.8 (2.22,3.52)	2.5 (2.09,2.91)	2.2 (1.91,2.64)

X	3.5 (2.70,4.61)	3.2 (2.50,4.19)	3.2 (2.21,4.66)
Day 28 A			
	7732.2 (6462.42,9251.52)	7368.8 (6210.80,8742.81)	3866.1 (2841.91,5259.43)
C	1143.9 (929.32,1407.98)	1095.4 (877.66,1367.12)	67.8 (39.69,115.84)
Y	2366.2 (1837.37,3047.14)	3010.0 (2490.61,3637.74)	676.9 (392.43,1167.54)
W	6533.4 (4868.00,8768.46)	5363.2 (3927.83,7323.21)	1127.5 (614.73,2067.93)
X	7548.3 (6442.99,8843.32)	8152.7 (6717.91,9893.84)	6.9 (3.82,12.56)
Day 84 A			
	4687.0 (3919.72,5604.44)	4488.3 (3600.74,5594.57)	2786.9 (2003.18,3877.24)
C	436.8 (342.33,557.34)	348.4 (272.51,445.33)	29.6 (18.73,46.87)
Y	1171.7 (891.95,1539.31)	1386.8 (1129.10,1703.21)	426.4 (252.21,720.93)
W	2555.6 (1839.63,3550.22)	2222.6 (1673.59,2951.80)	483.3 (242.96,961.24)
X	3511.3 (2934.73,4201.08)	3113.2 (2552.53,3796.93)	6.7 (3.73,11.91)
Day 112 A			
	6226.3 (5435.42,7132.33)	6166.7 (5375.47,7074.35)	4871.0 (3833.59,6189.12)
C	1366.9 (1173.58,1592.01)	1393.4 (1200.54,1617.35)	410.3 (324.93,518.11)
Y	3189.0 (2700.52,3765.84)	3266.7 (2800.84,3810.01)	1194.5 (809.00,1763.78)
W	8035.8 (6255.62,10322.51)	7056.4 (5622.17,8856.57)	2482.8 (1567.27,3933.27)
X	5363.2 (4523.30,6359.15)	6286.6 (5515.16,7165.86)	11.6 (6.35,21.34)

**For Serogroup C, all participants had same titer values at baseline in Adjuvanted MenFive and MenACWY-D arms.*

At 28 days after receipt of the first dose, >97% of the participants in the two MenFive groups had SBA titers of at least 128 against all five serogroups, whereas in the MenACWY-D group, SBA titers of at least 128 in at least 90% of participants were limited to serogroups A and W. The response in the MenACWY-D group against serogroup C was 54%, whereas it was 99% in the nonadjuvanted MenFive group.

Just before the receipt of the second dose (at day 84), at least 91% of the participants in the two MenFive groups still had SBA titers of at least 128 against all five serogroups. In the MenACWYD group, this threshold (≥128) was maintained in more than 90% of participants only for serogroup A; for serogroup C, 36% of the participants (95% CI, 25 to 48) had an SBA titer of at least 128.

At 28 days after receipt of the second dose (day 112), at least 99% of the participants in the two MenFive groups had an SBA titer of at least 128 against all five serogroups. In the MenACWY-D group, this threshold was met in at least 91% of the participants for serogroups A, C, W, and Y.

In this study, it was found that single dose of MenFive elicited immune responses that were similar to those observed with two doses of MenACWY-D. Adjuvanted MenFive provided no discernible benefit over nonadjuvanted MenFive.

Study ACYWX-03 (2-29 years' age)

The percentage of participants with seroresponse measured by rSBA 28 days after vaccination (Day 29) in the PP Population is presented in Table 7.

Non-inferiority of MenFive to the licensed MenACWY-D vaccine in terms of seroresponse on Day 29 was met.

In the MenFive group, the proportion of participants with a seroresponse on Day 29 in the overall population was highest for serogroups C, Y, W and X with a point estimate for seroresponse ≥97.0%; the seroresponse rate for serogroup A was 70.5%. In the MenACWY-D group, the proportion of participants with a seroreponse on Day 29 was ≥92.0% for serogroups C, Y and W; the seroresponse rate was 50.0% for serogroup A and 9.5% for serogroup X. The seroresponse rate in the MenFive group was higher than the MenACWY-D group for all serogroups in the overall population and in each age group.

Table 7: Seroresponse rates against serogroups A, C, Y, W and X, 28 days after vaccination - Per protocol population – Study ACYWX-03

Serogroup	**MenFive (N=1198) n (%) (95% CI)**	**MenACWY-D (N=595) n (%) (95% CI)**
A	814 (70.5) (67.8, 73.2)	286 (50.0) (45.8, 54.2)
C	1109 (97.9) (96.9, 98.6)	531 (95.5) (93.4, 97.1)
Y	1019 (97.0) (95.7, 97.9)	494 (92.0) (89.4, 94.1)
W	1081 (98.5) (97.6, 99.2)	520 (97.4) (95.6, 98.6)

Serogroup	**MenFive (N=1198) n (%) (95% CI)**	**MenACWY-D (N=595) n (%) (95% CI)**

X	1099 (97.2) (96.0, 98.1)	48 (9.5) (7.1, 12.4)

For percentage calculations, the denominator is the number of participants with non-missing values at baseline and postvaccination visits.
The 95% CIs for each treatment group were calculated by using the Clopper-Pearson method

The rSBA GMTs against serogroups A, C, Y, W and X on Day 29 in the PP Population are presented in Table 8.

Non-inferiority of MenFive to the licensed MenACWY-D vaccine in terms of rSBA GMTs on Day 29 was met.

In the MenFive group, the GMTs on Day 29 in the overall population were highest for serogroups W, Y and X; the lowest GMT was observed for serogroup C. With the exception of serogroup X, a similar profile was observed in the MenACWY-D group. The GMTs in the MenFive group were notably higher than the MenACWY-D group in the overall population and in each age group for all serogroups.

Table 8: rSBA Geometric Mean Titers per Serogroup - Per-Protocol Population - Study
ACYWX-03

Serogroup	**MenFive (N=1198) GMT (95% CI)**	**MenACWY-D (N=595) GMT (95% CI)**
Baseline		
A	1431.6 (1350.6, 1517.5)	1477.7 (1364.2, 1600.6)
C	8.0 (7.1, 9.0)	7.4 (6.2, 8.7)
Y	204.3 (180.3, 231.5)	215.3 (181.9, 254.9)
W	40.4 (34.2, 47.5)	45.8 (36.3, 57.7)
X	466.6 (417.2, 521.8)	488.2 (418.2, 570.0)
28 days after vaccination		
A	8009.9 (7631.7, 8407.0)	4729.7 (4420.0, 5061.2)
C	5587.2 (5123.7, 6092.5)	1854.9 (1619.6, 2124.4)
Y	10844.8 (10260.2, 11462.8)	4815.6 (4380.9, 5293.4)
W	28963.4 (26804.6, 31295.9)	12294.6 (10778.9, 14023.4)

X	31290.4 (29222.2, 33505.1)	737.1 (641.3, 847.4)

For each treatment, the GMT of antibodies measured by rSBA against each of the 5 serogroups and 95% CI were calculated by exponentiating the corresponding log_2-transformed mean and its 2-sided 95% CI limits on Day 29.

In the overall population, the percentage of participants in the MenFive group with rSBA titers ≥ 128 on Day 29 was at least 98.7% for each serogroup. A similar profile for rSBA titers ≥128 was observed for each age group. In the MenACWY-D group in the overall population, the percentage of participants with rSBA titers ≥ 128 was at least 94.6% for serogroups A, C, Y and W while it was 92.2% for serogroup X, with a similar profile observed for each age group.

Study ACYWX-04 (18-85 years' age)

This study demonstrated that MenFive is highly immunogenic and immunologically non-inferior to -MenACWY-D for all 5 serogroups. Consecutively manufactured 3 lots of NmCV-5 induced consistent immune responses.

The percentage of participants with seroresponse measured by rSBA on Day 29 in the modified Per Protocol (mPP) Population is presented in Table 9.

In the MenFive group, seroresponse rate was highest for serogroups C, Y, W and X with a point estimate of ≥ 90%; the seroresponse rate for serogroup A was 84.3%. In the MenACWY-D group, seroreponse rate was ≥ 89% for serogroups C, Y, and W; the seroresponse rate was 54.5% for serogroup A and 13.7% for serogroup X.

Table 9: Seroresponse rates against serogroups A, C, Y, W and X on Day 29 – mPP population – Study ACYWX-04

Serogroup	**MenFive (N=1170) n (%) (97.5% CI)**	**MenACWY-D (N=380) n (%) (97.5% CI)**
A	956 (84.3) (81.7, 86.7)	201 (54.5) (48.5, 60.3)
C	1051 (96.7) (95.3, 97.8)	309 (92.5) (88.6, 95.4)
Y	940 (93.6) (91.7, 95.2)	291 (89.8) (85.4, 93.3)
W	1040 (97.2) (95.8, 98.2)	325 (97.0) (94.2, 98.7)
X	945 (90.4) (88.2, 92.4)	40 (13.7) (9.5, 18.9)

For percentage calculations, the denominator is the number of participants with non-missing values at baseline and postvaccination visits.
Two sided 97.5 % CIs for each treatment group were calculated by using the Clopper-Pearson method

The rSBA GMTs against serogroups A, C, Y, W and X on Day 29 in the mPP Population are presented in Table 10.

In the MenFive group, GMTs on Day 29 ranged from 7016.9 (97.5% CI: 6475.7, 7603.4) for serogroup Y to 21225.3 (97.5% CI: 19061.0, 23635.2) for serogroup W. In the MenACWY-D group, GMTs on day 29 ranged from 3646.8 (97.5% CI: 3188.2, 4171.5) for serogroup Y to 11373.6 (97.5% CI: 9288.1, 13927.5) for serogroup W excluding serogroup X. GMTs in the MenFive group were notably higher than the MenACWY-D group for all serogroups.

Table 10: rSBA Geometric Mean Titers per Serogroup – mPP Population - Study ACYWX04

Serogroup	**MenFive (N=1170) GMT (97.5% CI)**	**MenACWY-D (N=380) GMT (97.5% CI)**
Baseline		
A	1270.9 (1152.6, 1401.3)	1349.7 (1134.6, 1605.4)
C	25.7 (21.8, 30.3)	32.6 (24.0, 44.3)
Y	133.1 (113.0, 156.7)	111.1 (82.4, 149.7)
W	42.5 (35.2, 51.5)	52.5 (37.2, 73.9)
X	176.6 (150.0, 208.0)	154.2 (112.7, 210.9)
28 days after vaccination		
A	14024.7 (13164.8, 14940.8)	5626.0 (5058.1, 6257.7)
C	9682.6 (8743.7, 10722.2)	4470.9 (3703.5, 5397.3)
Y	7016.9 (6475.7, 7603.4)	3646.8 (3188.2, 4171.5)
W	21225.3 (19061.0, 23635.2)	11373.6 (9288.1, 13927.5)
X	9587.1 (8590.4, 10699.4)	266.3 (199.4, 355.6)

Two-sided 97.5% CIs for GMT are estimated using log transformed Titer data and t-test. Antilog of log transformed mean of titers is taken to calculate GMT

of each treatment group. Antilog of 97.5% confidence limits of log transformed mean titers provides the 97.5% CI for the GMT of each treatment group.

The percentage of participants in the MenFive group with rSBA titers ≥128 on Day 29 was at least 98.3% for each serogroup. In the MenACWY-D group, the percentage of participants with rSBA titers ≥128 was at least 97.8% for each serogroup except for serogroup X (76.9%).

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Toxicity and local tolerance studies
In a repeat-dose toxicity study in rabbits, IM administration of MenFive was well tolerated. Nonadverse changes in dermal scores, globulin, and microscopic injection site findings were resolved, partially resolved and/or were trending toward recovery by the recovery necropsy.

Genotoxicity and Carcinogenicity:
In vitro genotoxicity and carcinogenicity studies were not performed.

Reproductive toxicity
In a reproductive and developmental toxicology study in rats, MenFive did not have any effects on maternal fertility or the pre- and post-natal development of offspring following maternal exposure during the pre-mating, gestation or lactation periods.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Powder
- Sucrose

- Sodium citrate dihydrate
- Tris buffer
- Reconstitution Diluent
- Sodium chloride
- Water for injection

6.2 Incompatibilities

In the absence of compatibility studies, this vaccine must not be mixed with other medicinal products.

6.3 Shelf-life

The expiry date of vaccine is indicated on the label and packaging.

Once opened, multi-dose vials should be used as soon as practically possible and within 6 hours when kept between +2°C and +8°C. All opened multidose vials of MenFive should be discarded at the end of immunization session or within six hours, whichever comes first.

6.4 Special precautions for storage

Store in a refrigerator (+2°C to +8°C). Do not freeze. Protect from light.
Opened multidose vial (After first use)
For storage conditions after first opening of the medicinal product, see section 6.3.

6.5 Nature and contents of container

MenFive is supplied as lyophilized powder in a single-dose or 5-dose vial along with diluent (i.e. 0.9% sodium chloride) in below listed presentations

1 dose - 0.5 mL per vial
5 dose - 2.5 mL per vial

6.6 Special Precautions for Disposal and Other Handling

Administration

The reconstituted vaccine is a colourless to pale yellow solution.

Freeze dried MenFive vaccine is reconstituted by aseptically injecting the entire volume of 0.9% sodium chloride diluent provided with the vaccine into the vial (single dose vial or 5-dose vial) containing the lyophilized MenACYWX component followed by gentle agitation to ensure the entire contents are solubilized. The reconstituted solution should be inspected visually prior to administration and discarded if particulate matter is observed.

Aseptic technique should be used for withdrawing the dose for administration. Each 0.5 mL dose of the vaccine is withdrawn into a syringe for injection and administered intramuscularly. A separate sterile needle and syringe should be used for each individual. Care should be taken to ensure a full 0.5 mL dose is administered. In the event that a full 0.5 mL dose cannot be extracted from the vial, the remaining volume should be discarded. Excess vaccine from multiple vials should not be pooled.

After first opening, multi-dose vials should be used as soon as practically possible and within 6 hours when kept between +2°C and +8°C. Any unused vaccine should be discarded.

To facilitate the traceability of the vaccine, the name and the batch number of the administered product must be recorded for each recipient.

Disposal

Any unused vaccine or waste material should be disposed of in accordance with local requirements. Spills should be disinfected with an appropriate disinfectant.

7 MARKETING AUTHORIZATION

Serum Institute of India Pvt. Ltd.

8 MARKETING AUTHORISATION NUMBER (S)

CTD 11130

9 DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION

23/08/2024

10 DATE OF REVISION OF THE TEXT

15/05/2025