HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use TRUMENBA safely and effectively. See full prescribing information for TRUMENBA.

TRUMENBA® (Meningococcal Group B Vaccine)
Suspension for intramuscular injection
Initial U.S. Approval: 2014

----------RECENT MAJOR CHANGES----------
Dosage and Administration, Dose and Schedule (2.1) [m/year]

----------INDICATIONS AND USAGE----------
- Trumenba is indicated for active immunization to prevent invasive disease caused by *Neisseria meningitidis* serogroup B. Trumenba is approved for use in individuals 10 through 25 years of age. (1)
- Approval of Trumenba is based on demonstration of immune response, as measured by serum bactericidal activity against four serogroup B strains representative of prevalent strains in the United States. The effectiveness of Trumenba against diverse serogroup B strains has not been confirmed. (1)

----------DOSAGE AND ADMINISTRATION----------
- For intramuscular use only. (2)
- **Three dose schedule:** Administer a dose (0.5 mL) at 0, 1-2, and 6 months. (2.1)
- **Two dose schedule:** Administer a dose (0.5 mL) at 0 and 6 months. (2.1)

----------DOSAGE FORMS AND STRENGTHS----------
- Suspension for intramuscular injection in 0.5 mL single-dose prefilled syringe. (3)

----------CONTRAINDICATIONS----------
- Severe allergic reaction after a previous dose of Trumenba. (4)

----------ADVERSE REACTIONS----------
The most common solicited adverse reactions were pain at the injection site (≥85%), fatigue (≥40%), headache (≥35%), muscle pain (≥30%), and chills (≥15%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer, Inc. at 1-800-438-1985 or VAERS at 1-800-822-7967 or http://vaers.hhs.gov.

----------USE IN SPECIFIC POPULATIONS----------
- **Pregnancy**: Trumenba should be used during pregnancy only if clearly needed. (8.1)
- **Pediatric Use:** Safety and effectiveness have not been established in children <10 years of age. In a clinical study, 90% of infants <12 months of age who were vaccinated with a reduced dosage formulation had fever. (8.4)

See 17 for PATIENT COUNSELING INFORMATION

Revised: m/2016

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Trumenba is indicated for active immunization to prevent invasive disease caused by *Neisseria meningitidis* serogroup B. Trumenba is approved for use in individuals 10 through 25 years of age.

Approval of Trumenba is based on demonstration of immune response, as measured by serum bactericidal activity against four serogroup B strains representative of prevalent strains in the United States. The effectiveness of Trumenba against diverse serogroup B strains has not been confirmed.

2 DOSAGE AND ADMINISTRATION

For intramuscular use only.

2.1 Dose and Schedule

Three dose schedule: Administer a dose (0.5 mL) at 0, 1-2, and 6 months.

Two dose schedule: Administer a dose (0.5 mL) at 0 and 6 months.

The choice of dosing schedule may depend on the risk of exposure and the patient's susceptibility to meningococcal serogroup B disease.

2.2 Administration

Shake syringe vigorously to ensure that a homogenous white suspension of Trumenba is obtained. Do not use the vaccine if it cannot be re-suspended. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not use if particulate matter or discoloration is found.

Inject each 0.5 mL dose intramuscularly, using a sterile needle attached to the supplied prefilled syringe. The preferred site for injection is the deltoid muscle of the upper arm. Do not mix Trumenba with any other vaccine in the same syringe.

2.3 Use of Trumenba with other Meningococcal Group B Vaccines

Sufficient data are not available on the safety and effectiveness of using Trumenba and other meningococcal group B vaccines interchangeably to complete the vaccination series.

3 DOSAGE FORMS AND STRENGTHS

Trumenba is a suspension for intramuscular injection in 0.5 mL single-dose prefilled syringe.

4 CONTRAINDICATIONS

Severe allergic reaction after a previous dose of Trumenba.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Allergic Reactions

Epinephrine and other appropriate agents used to manage immediate allergic reactions must be immediately available should an acute anaphylactic reaction occur following administration of Trumenba.

5.2 Altered Immunocompetence

Individuals with altered immunocompetence may have reduced immune responses to Trumenba.

6 ADVERSE REACTIONS

In clinical studies, the most common solicited adverse reactions were pain at the injection site (≥85%), fatigue (≥40%), headache (≥35%), muscle pain (≥30%), and chills (≥15%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in clinical practice.

The safety of Trumenba was evaluated in 4,282 subjects 11 through 25 years of age in 7 clinical studies (4 randomized controlled and 3 supportive non-controlled studies) conducted in the US, Europe, and Australia. A total of 4,250 adolescents (11 through 18 years of age) and 32 adults (19 through 25 years of age) received at least one dose of Trumenba. A total of 1,004 subjects 11 through 25 years of age in the control groups received saline placebo and/or one of the following vaccines: Human Papillomavirus Quadrivalent (Types 6, 11, 16, and 18) Vaccine, Recombinant [HPV4]; a non-US licensed tetanus toxoid, reduced diphtheria toxoid, acellular pertussis and inactivated polio virus vaccine; or Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Sanofi Pasteur Ltd.).

The safety evaluation in the 7 studies included an assessment of: (1) solicited local and systemic reactions, and use of antipyretic medication after each vaccination in an electronic diary maintained by the subject or the subject's parent/legal guardian; (2) spontaneous reports of adverse events (AEs), including serious adverse events (SAEs), throughout the study (day of vaccination through one month or 6 months after the last vaccination, depending on the study and safety parameter).

In controlled studies, demographic characteristics were generally similar with regard to gender, race, and ethnicity among subjects who received Trumenba and those who received control. Overall, across the 7 studies, among the subjects who received Trumenba, 56.1% were male and 44.0% were female, and the majority were White (90.8%) and non-Hispanic/non-Latino (91.4%).

Solicited Local and Systemic Adverse Reactions

In a randomized, active-controlled, observer-blinded, multicenter trial in the US, 1,982 adolescents 11 to <18 years of age received Trumenba at 0-, 2-, and 6-months. Subjects were randomized to 1 of 3 groups: Trumenba + HPV4 (Group 1), Trumenba + Saline (Group 2), Saline + HPV4 (Group 3). 81.6% of subjects were White, 13% were Black or African-American, 1.2% were Asian and 17.4% were Hispanic or Latino. Overall, 66.5% of subjects were male, 65.9% of participants were 11 to ≤14 years age and 34.1% were 15 to <18 years of age.

Local adverse reactions at the Trumenba injection site (Groups 1 and 2), and saline injection site (Group 3) were assessed in this study. Table 1 presents the percentage and severity of reported local adverse reactions within 7 days following each dose of Trumenba (Groups 1 and 2 combined) or saline control (Group 3).

Local adverse reactions were reported more frequently following Trumenba compared to saline (see Table 1).

Table 1: Percentage of US Subjects 11 to <18 Years of Age Reporting Local Adverse Reactions Within 7 Days After Each Vaccination[a]

	Trumenba[b] injection site			Saline[b] injection site		
Local Reaction	**Dose 1 N=1970**	**Dose 2 N=1826**	**Dose 3 N=1688**	**Dose 1 N=496**	**Dose 2 N=468**	**Dose 3 N=438**
Pain[c]						
Any[d]	92.8	86.1	84.5	36.9	29.1	23.3
Mild	42.5	49.9	44.1	33.1	24.6	20.8
Moderate	42.1	31.6	34.7	3.6	4.5	2.3
Severe	8.2	4.6	5.7	0.2	0.0	0.2
Redness[e]						
Any[d]	20.4	14.9	15.8	1.2	1.7	1.1
Mild	9.0	6.6	7.3	1.0	1.7	0.9
Moderate	9.1	7.0	7.0	0.2	0.0	0.2
Severe	2.2	1.3	1.4	0.0	0.0	0.0
Swelling[e]						
Any[d]	21.6	18.2	20.1	2.8	2.8	1.8
Mild	12.5	10.8	11.7	1.8	2.1	1.4
Moderate	8.5	7.1	8.2	1.0	0.6	0.5
Severe	0.5	0.3	0.2	0.0	0.0	0.0

[a] Study 1: National Clinical Trial (NCT) number NCT01461993.
[b] All vaccines and saline were administered at 0, 2 and 6 months.
[c] Mild (does not interfere with activity); Moderate (interferes with activity); Severe (prevents daily activity).
[d] "Any" is defined as the cumulative frequency of subjects who reported a reaction as "mild", "moderate" or "severe" within 7 days of vaccination.
[e] Mild (2.5-5.0 cm); Moderate (5.5-10.0 cm); Severe (>10.0 cm).

Table 2 presents the percentage of subjects who had at least one injection and who also reported a solicited systemic adverse reaction within 7 days of vaccination, by study group. These reactions resolved within 8 days in 90% of subjects. Fever (temperature ≥38.0°C) resolved within 3 days in 84% of subjects.

Table 2: Percentage of US Subjects 11 to <18 Years of Age Reporting Systemic Adverse Reactions and Use of Antipyretic Medications Within 7 Days After Each Vaccination[a]

	Group 1 Trumenba + HPV4[b]			Group 2 Trumenba + Saline[b]			Group 3 Saline + HPV4[b]		
	Dose 1 N=985	**Dose 2 N=919**	**Dose 3 N=842**	**Dose 1 N=985**	**Dose 2 N=907**	**Dose 3 N=846**	**Dose 1 N=496**	**Dose 2 N=468**	**Dose 3 N=438**
Systemic Reactions									
Fever (≥38.0°C)									
≥38.0°C[c]	8.3	2.1	2.1	6.4	1.3	1.1	0.8	0.9	0.7
38.0° to <38.5°C	4.9	1.2	1.1	3.7	1.1	0.8	0.4	0.4	0.2
38.5° to <39.0°C	2.5	0.4	0.6	1.5	0.1	0.1	0.0	0.2	0.0
39.0° to ≤40.0°C	0.6	0.3	0.4	1.0	0.1	0.1	0.2	0.2	0.2
Vomiting[d]									
Any[e,f]	7.8	2.8	2.4	7.4	2.4	2.5	3.4	3.0	1.6
Mild	5.8	2.1	2.1	5.3	1.4	1.8	3.2	2.4	0.9
Moderate	1.9	0.7	0.2	1.7	0.9	0.5	0.2	0.6	0.7

Severe	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Diarrhea[g]									
Any[e]	14.5	10.9	9.3	15.2	9.3	8.9	15.5	11.1	9.4
Mild	12.6	9.1	7.7	13.3	7.5	7.3	12.5	9.8	7.8
Moderate	1.7	1.6	1.1	1.7	1.8	1.2	2.6	1.3	1.6
Severe	0.2	0.1	0.5	0.2	0.0	0.4	0.4	0.0	0.0
Headache[h]									
Any[e]	56.9	44.8	41.0	54.8	40.8	34.8	43.1	36.5	27.4
Mild	37.7	32.9	30.0	36.1	28.3	24.0	33.3	25.4	21.0
Moderate	17.8	11.1	10.5	16.5	10.7	10.2	9.3	10.5	6.2
Severe	1.4	0.9	0.5	2.1	1.8	0.6	0.6	0.6	0.2
Fatigue[h]									
Any[e]	64.4	48.9	44.1	62.4	44.8	42.9	50.6	34.4	31.5
Mild	39.5	33.4	28.4	39.1	30.8	30.9	37.1	25.6	24.2
Moderate	20.6	12.8	14.3	19.7	12.3	10.9	13.1	7.9	7.1
Severe	4.3	2.6	1.4	3.7	1.7	1.2	0.4	0.9	0.2
Chills[h]									
Any[e]	30.3	19.2	17.5	29.0	17.4	15.6	16.7	12.0	8.2
Mild	21.5	13.8	13.1	22.0	13.6	12.5	13.9	9.6	7.1
Moderate	7.4	4.1	3.7	5.6	2.9	3.0	2.6	2.1	1.1
Severe	1.3	1.2	0.7	1.4	1.0	0.1	0.2	0.2	0.0
Muscle pain (other than muscle pain at the injection site)[h]									
Any[e]	41.1	36.6	35.3	42.4	30.5	30.9	28.6	24.6	20.8
Mild	24.7	25.0	22.2	25.7	19.8	21.3	23.4	19.4	16.2
Moderate	13.3	10.2	11.2	13.9	9.3	8.5	4.6	4.9	3.9
Severe	3.1	1.3	1.9	2.8	1.4	1.1	0.6	0.2	0.7
Joint pain[h]									
Any[e]	21.6	15.5	19.2	21.6	15.4	17.0	13.7	12.2	11.0
Mild	15.7	11.1	13.4	14.7	11.8	13.7	10.9	9.8	8.7
Moderate	5.0	3.8	4.9	5.9	3.0	3.1	2.8	2.4	1.6
Severe	0.9	0.5	1.0	1.0	0.7	0.2	0.0	0.0	0.7
Use of Antipyretic medication	26.3	16.1	16.5	27.0	17.5	17.0	13.3	13.9	6.6

[a] Study 1: NCT01461993.

[b] All vaccines and saline were administered at 0, 2 and 6 months.

[c] Eight subjects reported 9 episodes of fever which could not be further classified as 38.0° to <38.5°C, 38.5° to <39.0°C, 39.0° to ≤40.0°C or >40.0°C. 3 of these episodes occurred in Group 1, dose 1; 2 occurred in Group 2, dose 1; 1 occurred in Group 3, dose 1; 1 occurred in Group 1, dose 2; 1 occurred in Group 1, dose 3; and 1 occurred in Group 3, dose 3.

[d] Mild (1-2 times in 24 hours); Moderate (>2 times in 24 hours); Severe (requires IV hydration).

[e] "Any" is defined as the cumulative frequency of subjects who reported a reaction as "mild", "moderate" or "severe" within 7 days of vaccination.

[f] Nine subjects reported vomiting which could not be further classified. 1 of these reports occurred in Group 1, dose 1; 4 occurred in Group 2, dose 1; 1 occurred in Group 1, dose 2; 1 occurred in Group 2, dose 2; and 2 occurred in Group 2, dose 3.

[g] Mild (2-3 loose stools in 24 hours); Moderate (4-5 loose stools in 24 hours); Severe (6 or more loose stools in 24 hours).

[h] Mild (does not interfere with activity); Moderate (interferes with activity); Severe (prevents daily activity).

The frequencies of adverse events were highest after the first dose regardless of the schedule. The frequencies of adverse events after subsequent doses were similar.

Serious Adverse Events

Overall in clinical studies in which 4282 subjects 11 through 25 years of age received at least one dose of Trumenba, serious adverse events (SAEs) were reported by 88 (2.0%) subjects.

Among the 4 controlled studies (Trumenba N=2557, control N=1004), SAEs were reported by 44 (1.7%) subjects and by 16 (1.6%) subjects who received at least one dose of Trumenba or comparator study product, respectively.

Non-serious Adverse Events

Overall in clinical studies in which 4282 subjects 11 through 25 years of age received Trumenba, non-serious AEs within 30 days after any dose were reported in 1049 (24.5%) subjects. Among the 4 controlled studies (Trumenba N=2557, control N=1004), AEs that occurred within 30 days of vaccination were reported in 739 (28.9%) subjects who received Trumenba and 313 (31.2%) subjects in the control group, for individuals who received at least one dose. AEs that occurred at a frequency of at least 2% and were more frequently observed in subjects who received Trumenba than subjects in the control group were injection site pain and headache.

7 DRUG INTERACTIONS

In a clinical trial, Trumenba was administered concomitantly with HPV4 in adolescents 11 to <18 years of age *[see Clinical Studies (14.2) and Adverse Reactions (6.1)]*.

Data are insufficient to assess the safety and immunogenicity of concomitant administration of Trumenba with meningococcal serogroups A, C, Y, W conjugate vaccine or Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine, Adsorbed.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category B

Reproduction studies have been performed in female rabbits at a dose approximately 17 times the human dose (on a mg/kg basis) and revealed no evidence of impaired female fertility or harm to the fetus due to Trumenba. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproductive studies are not always predictive of the human response, this vaccine should be used during pregnancy only if clearly needed.

8.3 Nursing Mothers

It is not known whether Trumenba is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Trumenba is administered to a nursing woman.

8.4 Pediatric Use

Safety and effectiveness have not been established in children <10 years of age. In a clinical study, 90% of infants <12 months of age who were vaccinated with a reduced dosage formulation had fever.

8.5 Geriatric Use

Safety and effectiveness of Trumenba in adults older than 65 years of age have not been established.

11 DESCRIPTION

Trumenba is a sterile suspension composed of two recombinant lipidated factor H binding protein (fHBP) variants from *N. meningitidis* serogroup B, one from fHBP subfamily A and one from subfamily B (A05 and B01, respectively).[1] The proteins are individually produced in *E. coli*. Production strains are grown in defined fermentation growth media to a specific density. The recombinant proteins are extracted from the production strains and purified through a series of column chromatography steps. Polysorbate 80 (PS80) is added to the drug substances and is present in the final drug product.

Each 0.5 mL dose contains 60 micrograms of each fHBP variant (total of 120 micrograms of protein), 0.018 mg of PS80 and 0.25 mg of Al^{3+} as $AlPO_4$ in 10 mM histidine buffered saline at pH 6.0.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Protection against invasive meningococcal disease is conferred mainly by complement-mediated antibody-dependent killing of *N. meningitidis*. The effectiveness of Trumenba was assessed by measuring serum bactericidal activity using human complement (hSBA).

fHBP is one of many proteins found on the surface of meningococci and contributes to the ability of the bacterium to avoid host defenses. fHBPs can be categorized into two immunologically distinct subfamilies, A and B.[1] The susceptibility of serogroup B meningococci to complement-mediated antibody-dependent killing following vaccination with Trumenba is dependent on both the antigenic similarity of the bacterial and vaccine fHBPs, as well as the amount of fHBP expressed on the surface of the invading meningococci.

13 NONCLINICAL TOXICOLOGY

Trumenba has not been evaluated for carcinogenic or mutagenic potential or impairment of fertility in males.

14 CLINICAL STUDIES

In two randomized studies, the immunogenicity of Trumenba was evaluated in individuals 11 to <18 years of age in the US (Study 1) and in individuals 11 to <19 years of age in Europe (Study 2). Serum bactericidal antibodies were measured with hSBA assays that used each of four meningococcal group B strains. The four test strains express fHBP variants representing the two subfamilies (A and B) and, when taken together, are representative of prevalent strains in the US and Europe. The studies assessed the proportions of subjects with a 4-fold or greater increase in hSBA titer for each of the four strains, and the proportion of subjects who achieved a titer greater than or equal to the lower limit of quantitation (LLOQ) of the assay for all four strains (composite response). The LLOQ was defined as the lowest amount of the antibody in a sample that can be reliably quantified.

14.1 Immunogenicity

In Study 1, Group 1 received Trumenba + HPV4, Group 2 received Trumenba + Saline, and Group 3 received Saline + HPV4 *[see Adverse reactions (6.0)]*. The hSBA responses observed after the second dose and completion of the 3-dose series are presented in Table 3.

Table 3: Percentage of US Individuals 11 to <18 Years of Age With a ≥4-Fold Increase in hSBA Titer and Composite Response [a,b]

	Group 1[c]	Group 2[c]
	Trumenba + HPV4[d]	Trumenba + Saline[d]
fHBP Variant[e]	**% (95% CI)[f]**	**% (95% CI)[f]**
≥4-fold Increase[g]		
A22		
Dose 2	73.3 (70.2, 76.4)	74.0 (70.9, 77.0)
Dose 3	85.3 (82.6, 87.7)	86.4 (83.8, 88.7)
A56		
Dose 2	92.8 (90.8, 94.5)	92.7 (90.7, 94.5)
Dose 3	95.0 (93.2, 96.5)	95.3 (93.6, 96.8)
B24		
Dose 2	61.8 (58.4, 65.2)	63.5 (60.1, 66.9)
Dose 3	83.4 (80.5, 85.9)	84.8 (82.0, 87.2)
B44		
Dose 2	46.0 (42.5, 49.5)	48.8 (45.3, 52.3)
Dose 3	77.0 (73.9, 79.9)	80.7 (77.8, 83.4)
Composite Response[g,h]		
Before Dose 1	0.4 (0.1, 1.1)	0.7 (0.2, 1.6)
Dose 2	50.1 (46.5, 53.8)	52.6 (48.9, 56.2)
Dose 3	81.0 (78.0, 83.7)	83.9 (81.1, 86.4)

Abbreviations: CI = Confidence interval; hSBA = Serum bactericidal activity measured using human complement; LLOQ = Lower limit of quantitation.

Note: LLOQ = 1:16 for PMB80 (A22); 1:8 for PMB2001 (A56), PMB2948 (B24), and PMB2707 (B44).

Note: The ≥4-fold increase is defined as follows: (1) For subjects with a baseline hSBA titer <1:4, a ≥4-fold increase was defined as an hSBA titer ≥1:16. (2) For subjects with a baseline hSBA titer ≥1:4, a ≥4-fold increase was defined as an hSBA titer ≥4 times the LLOQ or ≥4 times the baseline titer, whichever was higher.

[a] Evaluable Immunogenicity Populations. Dose #2 data include subjects who received two doses, irrespective of whether they received the third dose.

[b] Study 1: NCT01461993.

[c] The denominators ranged from 752–818 after dose 2 and 742–792 after dose 3 for Group 1; 757–827 after dose 2 and 730–788 after dose 3 for Group 2, depending on strain and dose .

[d] All vaccines and saline were administered at 0, 2 and 6 months.

[e] The strains expressing variant A22, A56, B24, and B44 correspond to strains PMB80, PMB2001, PMB2948, and PMB2707, respectively.

[f] Exact 2-sided confidence interval (Clopper and Pearson) based upon the observed proportion of subjects.

[g] For the second and third doses, serum was obtained approximately 1 month after vaccination.

[h] Composite Response = hSBA ≥LLOQ for all 4 primary Meningococcal B strains.

In Study 2, Trumenba was administered according to the following schedules: Group 1 (0, 1 and 6 months); Group 2 (0, 2 and 6 months); Group 3 (0 and 6 months); Group 4 (0 and 2 months); Group 5 (0 and 4 months) *[see Adverse Reactions (6.0)]*. The hSBA responses observed after the second dose in Groups 1, 2 and 3, and completion of the 3-dose series in Group 1 and 2 are presented in Table 4.

Table 4: Percentage of European Individuals 11 to <19 Years of Age With a ≥4-Fold Increase in hSBA Titer and Composite Response[a,b]

	Group 1	Group 2	Group 3
	3-dose schedule (0-, 1- and 6-months)[c]	3-dose schedule (0-, 2- and 6-months)[d]	2-dose schedule (0- and 6-months)[e]
fHBP Variant[f,g]	**% (95% CI)[h]**	**% (95% CI)[h]**	**% (95% CI)[h]**
≥4-fold Increase			
PMB80 (A22)			
Dose 2	58.8 (51.4, 66.0)	72.5 (66.4, 78.0)	82.3 (76.3, 87.3)

Dose 3	77.6 (70.9, 83.4)	87.7 (81.6, 92.3)	NA
PMB2001 (A56)			
Dose 2	87.8 (82.2, 92.2)	90.7 (86.2, 94.1)	90.1 (85.1, 93.8)
Dose 3	91.2 (86.1, 94.9)	93.8 (88.8, 97.0)	NA
PMB2948 (B24)			
Dose 2	51.1 (43.6, 58.5)	54.2 (47.7, 60.7)	64.5 (57.4, 71.1)
Dose 3	74.1 (67.1, 80.2)	78.3 (71.1, 84.4)	NA
PMB2707 (B44)			
Dose 2	48.1 (40.7, 55.6)	53.4 (46.8, 59.9)	66.0 (58.9, 72.6)
Dose 3	80.9 (74.5, 86.2)	78.6 (71.4, 84.7)	NA
Composite response[g,i]			
Before Dose 1	4.6 (2.0, 8.8)	2.2 (0.7, 5.0)	1.5 (0.3, 4.4)
Dose 2	52.0 (44.3, 59.7)	52.0 (45.3, 58.6)	72.9 (65.9, 79.1)
Dose 3	80.3 (73.7, 85.9)	81.8 (74.9, 87.4)	NA

Abbreviations: CI= Confidence Interval; fHBP = factor H binding protein; hSBA = serum bactericidal assay using human complement; LLOQ = lower limit of quantitation; NA = Not Applicable

Note: LLOQ = 1:16 for PMB80 (A22) and 1:8 for PMB2001 (A56), PMB2948 (B24), and PMB2707 (B44).

Note: The ≥4-fold increase is defined as follows: (1) For subjects with a baseline hSBA titer <1:4, a ≥4-fold increase was defined as an hSBA titer ≥1:16. (2) For subjects with a baseline hSBA titer ≥1:4, a ≥4-fold increase was defined as an hSBA titer ≥4 times the LLOQ or ≥4 times the baseline titer, whichever was higher.

[a] Per-Schedule Evaluable Populations. Dose #2 data include subjects who received two doses, irrespective of whether they received the third dose.

[b] Study 2: NCT01299480.

[c] Group 1 (0-, 1-, and 6 -months). The denominators ranged from 173-187 after dose 2 and 178-188 after dose 3, depending on the strain.

[d] Group 2 (0-, 2-, and 6 -months). The denominators ranged from 229-240 after dose 2 and 159-162 after dose 3, depending on the strain.

[e] Group 3 (0- and 6 -months). The denominators ranged from 188-203 after dose 2, depending on the strain.

[f] The strains expressing variant A22, A56, B24, and B44 correspond to strains PMB80, PMB2001, PMB2948, and PMB2707, respectively.

[g] For the second and third doses, serum was obtained approximately 1 month after vaccination.

[h] Exact 2-sided confidence interval (Clopper and Pearson) based upon the observed proportion of subjects.

[i] Composite Response = hSBA ≥LLOQ for all 4 primary Meningococcal B strains.

14.2 Concomitant Vaccine Administration

In Study 1 conducted in the US, the immunogenicity of concomitantly administered Trumenba and HPV4 was evaluated in adolescents 11 to <18 years of age *[see Clinical Studies (14.1) and Adverse Reactions (6.1)]*. Immune responses were evaluated by comparisons of geometric mean titer [GMT] for each HPV type at 1 month after the third HPV4 vaccination (Group 1 vs. Group 3), and hSBA GMTs using two meningococcal serogroup B strains [variants A22 and B24] 1 month after the third Trumenba vaccination (Group 1 vs. Group 2).

The noninferiority criteria for comparisons of the GMT ratio (lower limit of the 2-sided 95% confidence interval of the GMT ratio >0.67) were met for three HPV types (6, 11 and 16) and for the meningococcal serogroup B strains. For HPV-18, the lower bound of the 95% confidence interval (CI) for the GMT ratio was 0.62 at one month after the third HPV4 vaccination.

15 REFERENCES

1. Wang X, et al. Prevalence and genetic diversity of candidate vaccine antigens among invasive *Neisseria meningitidis* isolates in the United States. Vaccine 2011; 29:4739-4744.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

Trumenba is supplied in the following strengths and package configurations:

Prefilled Syringe, 1 Dose (10 per package) – NDC 0005-0100-10.

Prefilled Syringe, 1 Dose (5 per package) – NDC 0005-0100-05.

After shipping, Trumenba may arrive at temperatures between 2°C to 25°C (36°F to 77°F).

The tip cap and rubber plunger of the prefilled syringe are not made with natural rubber latex.

16.2 Storage and Handling

Upon receipt, store refrigerated at 2°C to 8°C (36°F to 46°F).

Store syringes in the refrigerator horizontally (laying flat on the shelf) to minimize the re-dispersion time.

Do not freeze. Discard if the vaccine has been frozen.

17 PATIENT COUNSELING INFORMATION

Prior to administration of this vaccine, the healthcare professional should inform the individual, parent, guardian, or other responsible adult of the following:

- The importance of completing the immunization series.
- Report any suspected adverse reactions to a healthcare professional.

Provide the Vaccine Information Statements, which are available free of charge at the Centers for Disease Control and Prevention (CDC) website (www.cdc.gov/vaccines).

Manufactured by

Pfizer

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A subsidiary of Pfizer Inc, Philadelphia, PA 19101

US Govt. License No. 3

LAB-0722-3.6
CPT Code 90621