PRODUCT INFORMATION

TRUMENBA[â]

NAME OF THE MEDICINE

Meningococcal group B vaccine

DESCRIPTION

Trumenba is a sterile homogeneous white suspension composed of two recombinant lipidated factor H binding protein (fHBP) variants from *Neisseria meningitidis* serogroup B, one from fHBP subfamily A and one from subfamily B (A05 and B01, respectively).

Active ingredients

Each 0.5 mL dose contains:

Neisseria meningitidis serogroup B recombinant lipidated-

factor H binding protein subfamily A	60 µg
factor H binding protein subfamily B	60 µg

Excipients

Sodium chloride, histidine, water for injections, aluminium phosphate and polysorbate 80.

PHARMACOLOGY

Mechanism of Action

Protection against invasive meningococcal disease is mediated by serum bactericidal antibodies to bacterial surface antigens. Bactericidal antibodies act in concert with human complement to kill meningococci. This process is measured in vitro with serum bactericidal assay using human complement (hSBA) for serogroup B. A positive response in SBA is an accepted correlate of protection from meningococcal disease.

Trumenba [bivalent rLP2086] is a vaccine composed of two recombinant lipidated factor H binding proteins (fHBPs) and prevents serogroup B disease by inducing broadly protective bactericidal antibody responses against epidemiologically diverse serogroup B strains. fHBP is found on the surface of meningococcal bacteria and is essential for bacteria to avoid host immune defenses. fHBPs segregate into two immunologically distinct subfamilies, A and B, and >95% of serogroup B strains express fHBPs from either subfamily.

Vaccination with Trumenba, which contains one fHBP each from subfamily A and B, elicits bactericidal antibodies directed against fHBP found on the surface of *N. meningitidis* serogroup B strains.

CLINICAL TRIALS

The efficacy of Trumenba has not been evaluated through clinical trials. Vaccine efficacy has been inferred by demonstrating the induction of serum bactericidal antibody responses to four meningococcal group B test strains (see CLINICAL TRIALS, Immunogenicity). The four test strains express fHBP variants representing the two subfamilies (A and B) and, when taken together, are representative of prevalent strains causing invasive disease. The studies assessed the proportions of subjects with a 4-fold or greater increase from baseline in hSBA titer for each of the four strains and for the four strains combined (composite response), the proportion of subjects who achieved a titer greater than or equal to 1:8 (3 strains) or 1:16 (1 strain).

Immunogenicity

The immunogenicity of Trumenba following two or three vaccinations was evaluated in individuals 11 to 18 years of age in Europe (Study B1971012) and following three vaccinations in individuals 10 to 25 years of age globally (Studies B1971009 and B1971016).

In Study B1971012, 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). The hSBA responses observed after the second or third dose are presented in Table 1.

Table 1. Immune Responses Among Individuals 11 to 18 Years of Age Administered Trumenba After Various 2- and 3-Dose Schedules (Study B1971012)[a,b]

		Group 1	Group 2	Group 3	Group 4	Group 5
		(0, 1, and 6 Months)[c]	(0, 2, and 6 Months)[d]	(0 and 6 Months)[e]	(0 and 2 Months)[f]	(0 and 4 Months)[g]
fHBP Variant[h,i]		%/GMT (95% CI)[j]	%/GMT (95% CI)[j]	%/GMT (95% CI)[j]	%/GMT (95% CI)[j]	%/GMT (95% CI)[j]
PMB80 (A22)						
	Proportion of subjects who achieved ≥ 4-Fold rise in hSBA titer					
	Dose 2	58.8 (51.4, 66.0)	72.5 (66.4, 78.0)	82.3 (76.3, 87.3)	74.3 (66.9,80.7)	75.0 (63.7, 84.2)
	Dose 3	77.6 (70.9, 83.4)	87.7 (81.6, 92.3)	--	--	--
	hSBA GMT					
	Before Dose 1	12.0 (10.9, 13.3)	10.6 (9.6, 11.7)	10.7 (9.8, 11.6)	11.3 (10.1, 12.6)	11.9 (9.9, 14.4)
	Dose 2	32.2 (27.6, 37.7)	36.5 (31.8, 42.0)	48.9 (43.2, 55.3)	38.2 (32.8, 44.7)	44.1 (35.3, 55.1)
	Dose 3	60.1 (52.2, 69.3)	62.4 (54.7, 71.2)	--	--	--
PMB2001 (A56)						
	Proportion of subjects who achieved ≥ 4-Fold rise in hSBA titer					
	Dose 2	87.8 (82.2, 92.2)	90.7 (86.2, 94.1)	90.1 (85.1, 93.8)	93.3 (88.2,96.6)	90.9 (82.2, 96.3)
	Dose 3	91.2 (86.1, 94.9)	93.8 (88.8, 97.0)	--	--	--

	hSBA GMT					
	Before Dose 1	7.0 (5.9, 8.3)	6.4 (5.6, 7.5)	6.3 (5.5, 7.2)	6.2 (5.3, 7.2)	6.6 (5.2, 8.4)
	Dose 2	91.0 (78.4, 105.7)	94.5 (80.9, 110.3)	113.9 (99.5, 130.4)	97.7 (84.6, 112.8)	114.7 (90.2, 145.8)
	Dose 3	147.2 (127.5, 170.0)	152.7 (130.7, 178.5)	--	--	--

PMB2948 (B24)						
	Proportion of subjects who achieved ≥ 4-Fold rise in hSBA titer					
	Dose 2	51.1 (43.6, 58.5)	54.2 (47.7, 60.7)	64.5 (57.4, 71.1)	56.1 (48.4,63.7)	55.0 (43.5, 66.2)
	Dose 3	74.1 (67.1, 80.2)	78.3 (71.1, 84.4)	--	--	--
	hSBA GMT					
	Before Dose 1	5.7 (5.1, 6.5)	5.3 (4.8, 6.0)	4.9 (4.5, 5.4)	5.0 (4.6, 5.6)	5.3 (4.5, 6.3)
	Dose 2	16.4 (13.9, 19.5)	16.2 (13.7, 19.2)	19.0 (16.3, 22.1)	17.4 (14.5, 20.7)	15.7 (12.4, 20.0)
	Dose 3	28.8 (24.4, 34.1)	27.3 (23.5, 31.8)	--	--	--
PMB2707 (B44)						
	Proportion of subjects who achieved ≥ 4-Fold rise in hSBA titer					
	Dose 2	48.1 (40.7, 55.6)	53.4 (46.8, 59.9)	66.0 (58.9, 72.6)	57.2 (49.3, 64.9)	60.5 (49.0, 71.2)
	Dose 3	80.9 (74.5, 86.2)	78.6 (71.4, 84.7)	--	--	--
	hSBA GMT					
	Before Dose 1	4.5 (4.2, 4.8)	4.3 (4.1, 4.5)	4.3 (4.1, 4.6)	4.7 (4.3, 5.2)	4.5 (4.1, 5.1)
	Dose 2	15.7 (12.8, 19.4)	14.5 (12.0, 17.4)	20.9 (17.4, 25.1)	17.2 (14.0, 21.1)	17.6 (13.4, 23.0)
	Dose 3	39.0 (32.2, 47.4)	32.1 26.4, 39.1)	--	--	--
Composite response (Proportion of subjects who achieved hSBA ≥ LLOQ for all 4 hSBA strains combined)[i,k]						
	Before Dose 1	4.6 (2.0, 8.8)	2.2 (0.7, 5.0)	1.5 (0.3, 4.4)	5.6 (2.6, 10.4)	4.2 (0.9, 11.7)
	Dose 2	52.0 (44.3, 59.7)	52.0 (45.3, 58.6)	72.9 (65.9, 79.1)	57.8 (49.7, 65.5)	59.0 (47.3, 70.0)
	Dose 3	80.3 (73.7, 85.9)	81.8 (74.9, 87.4)	--	--	--

Abbreviations: fHBP = factor H binding protein; GMT = geometric mean titer; hSBA = serum bactericidal assay using human complement; LLOQ = lower limit of quantitation.

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 response was defined as an hSBA titer ≥ 1:16. (2) For subjects with a baseline hSBA titer ≥ 1:4, a 4-fold response 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. For the GMT endpoint, for Groups 1 and 2, the 3-dose per-schedule evaluable population was used.

b NCT01299480.

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

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

e Group 3 (0 and 6 months). The denominators ranged from 188 to 203 after Dose 2.

f Group 4 (0 and 2 months). The denominators ranged from 161 to 171 after Dose 2.

g Group 5 (0 and 4 months). The denominators ranged from 78 to 81 after Dose 2.

h The strains expressing variants A22, A56, B24, and B44 correspond to strains PMB80, PMB2001, PMB2948, and PMB2707, respectively.

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

j Exact 2-sided confidence interval (Clopper and Pearson) based upon the observed proportion of subjects. For GMTs, CIs are back transformations of confidence levels based on the Student t distribution for the mean logarithm of the hSBA titers.

k Composite response = hSBA ≥ LLOQ for all 4 primary meningococcal B strains combined.

Study B1971009 was a Phase 3, randomised, active-controlled, observer-blinded, multicenter trial in which subjects aged 10 to 18 years received 1 of 3 lots (Groups 1, 2, and

3) of Trumenba or the active control hepatitis A virus (HAV) vaccine/saline. The study assessed the safety, tolerability, immunogenicity, and demonstration of the lot consistency of 3 lots of Trumenba administered on a 0-, 2-, and 6-month schedule. The hSBA responses observed after the second and third doses in Group 1 are presented in Table 2. Results from Groups 2 and 3 are not presented, as only 2 representative strains were evaluated. Similar results were observed in Groups 2 and 3 as observed in Group 1.

Study B1971016 was a Phase 3, randomised, placebo-controlled, observer-blinded, multicenter trial in which subjects 18 to 25 years of age were assigned to 2 groups in a 3:1 ratio (Group 1: Group 2). Group 1 received Trumenba at months 0, 2, and 6. Group 2 received saline at months 0, 2, and 6. The hSBA responses observed after the second and third doses in Group 1 are presented in Table 2.

Table 2. Immune Responses Among Individuals 10 to 25 Years of Age Administered Trumenba on a 0-, 2-, and 6- Month Schedule (Studies 1009 and 1016)[a,b,c,d]

fHBP Variant[f,g]		Study B1971009 Aged 10 to 18 Years %/GMT[e] (95% CI)[h]	Study B1971016 Aged 18 to 25 Years %/GMT[e] (95% CI)[h]
PMB80 (A22)			
	Proportion of subjects who achieved ≥ 4-Fold rise in hSBA titer		
	Dose 2	73.8 (71.2, 76.2)	66.9 (64.6, 69.2)
	Dose 3	83.2 (81.0, 85.2)	80.5 (78.6, 82.4)
	hSBA GMT		
	Before Dose 1	12.6 (12.1, 13.1)	12.8 (12.3, 13.3)
	Dose 2	50.4 (47.8, 53.1)	49.0 (46.2, 52.1)
	Dose 3	86.8 (82.3, 91.5)	74.3 (70.2, 78.6)
PMB2001 (A56)			
	Proportion of subjects who achieved ≥ 4-Fold rise in hSBA titer		
	Dose 2	84.8 (82.5, 86.8)	85.9 (84.1, 87.5)
	Dose 3	90.2 (88.4, 91.9)	90.0 (88.4, 91.4)
	hSBA GMT		
	Before Dose 1	8.4 (7.8, 9.1)	8.8 (8.3, 9.3)
	Dose 2	131.2 (124.0, 138.7)	114.3 (107.9, 121.0)
	Dose 3	222.5 (210.1, 235.6)	176.7 (167.8, 186.1)
PMB2948 (B24)			
	Proportion of subjects who achieved ≥ 4-Fold rise in hSBA titer		
	Dose 2	56.2 (53.3, 59.0)	67.9 (65.6, 70.2)
	Dose 3	79.8 (77.4, 82.0)	79.3 (77.3, 81.2)
	hSBA GMT		
	Before Dose 1	4.5 (4.4, 4.6)	7.6 (7.3, 8.0)
	Dose 2	14.3 (13.5, 15.3)	35.8 (33.7, 38.2)
	Dose 3	24.1 (22.7, 25.5)	49.5 (46.8, 52.4)

PMB2707 (B44)			
	Proportion of subjects who achieved ≥ 4-Fold rise in hSBA titer		
	Dose 2	55.9 (53.0, 58.7)	55.5 (53.1, 57.9)
	Dose 3	85.9 (83.8, 87.8)	79.6 (77.6, 81.5)
	hSBA GMT		
	Before Dose 1	4.3 (4.2, 4.3)	4.8 (4.7, 4.9)
	Dose 2	17.1 (15.8, 18.6)	22.6 (20.9, 24.4)
	Dose 3	50.9 (47.0, 55.2)	47.6 (44.2, 51.3)
Composite hSBA response (Proportion of subjects who achieved hSBA ≥ LLOQ for all 4 hSBA strains combined) [i]			
	Before Dose 1	1.1 (0.6, 1.9)	7.3 (6.0, 8.6)
	Dose 2	54.1 (51.1, 57.0)	64.5 (62.1, 66.8)
	Dose 3	83.5 (81.3, 85.6)	84.9 (83.1, 86.6)

Abbreviations: fHBP = factor H binding protein; GMT = geometric mean titer; hSBA = serum bactericidal assay using human complement; LLOQ = lower limit of quantitation; LOD = limit of detection.
Note: LLOQ = 1:16 for A22; 1:8 for A56, B24, and B44.
Note: The 4-fold increase is defined as follows: (1) For subjects with a baseline hSBA titer below the LOD (hSBA titer < 1:4), a response is defined as an hSBA titer ≥ 1:16 or the LLOQ (whichever titer is higher). (2) For subjects with a baseline hSBA titer ≥ LOD and < LLOQ, a response is defined as an hSBA titer ≥ 4 times the LLOQ. (3) For subjects with a baseline hSBA titer ≥ LLOQ, a response is defined as an hSBA titer ≥ 4 times the baseline titer.
a Evaluable immunogenicity population.
b Study B1971009 = NCT01830855 and Study B1971016 = NCT01352845.
c Study B1971009: Group 1 (0, 2, and 6 months). The denominators ranged from 1122 to 1223 (4-fold and composite responses) and 1204 to 1263 (GMTs) after Dose 2; 1128 to 1235 (4-fold and composite responses) and 1210 to 1266 (GMTs) after Dose 3, depending on the strain.
d Study B1971016: Group 1 (0, 2, and 6 months). The denominators ranged from 1620 to 1686 (4-fold and composite) and 1685 to 1701 (GMTs) after Dose 2; 1642 to 1696 (4-fold and composite) and 1702 to 1714 (GMTs) after Dose 3, depending on the strain.
e GMTs were calculated using all subjects with valid and determinate hSBA titers at the given time point.
f The strains expressing variants 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-Pearson method) based upon the observed proportion of subjects. For GMTs, CIs are back transformations of confidence levels based on the Student t distribution for the mean logarithm of the hSBA titers
i Composite response = hSBA ≥ LLOQ for all 4 primary meningococcal B strains.

In Studies B1971009 and B1971016, the proportion of subjects achieving a defined hSBA titer after 2 and 3 doses of Trumenba, administered on a 0-, 2-, and 6-month schedule, was evaluated against a panel of 10 additional strains, each expressing a different fHBP variant (Table 3).

Table 3. Immune Responses Among Individuals 10 to 25 Years of Age With a Defined hSBA Titer Against 10 Additional Strains (Study B1971009 and Study B1971016)[a,b]

	Study B1971009	**Study B1971016**
	(10 to 18 Years of Age) (0, 2, and 6 Months)[c]	**(18 to 25 Years of Age) (0, 2, and 6 Months)[d]**
fHBP Variant[e,f]	**(%) (95% CI)[g]**	**(%) (95% CI)[g]**
Proportion of subjects who achieved hSBA ≥ LLOQ **(LLOQ = hSBA titer 1:8)**		

Table 3. Immune Responses Among Individuals 10 to 25 Years of Age With a Defined hSBA Titer Against 10 Additional Strains (Study B1971009 and Study B1971016)[a,b]		
PMB3040 (A07)		
Dose 2	93.8 (86.9, 97.7)	97.9 (92.6, 99.7)
Dose 3	96.4 (93.5, 98.3)	95.7 (92.6, 97.7)
PMB1672 (A15)		
Dose 2	65.6 (55.0, 75.1)	83.2 (74.1, 90.1)
Dose 3	87.2 (82.6, 91.0)	91.8 (87.9, 94.7)
PMB3175 (A29)		
Dose 2	100.0 (96.3, 100.0)	96.8 (91.0, 99.3)
Dose 3	98.6 (96.4, 99.6)	99.3 (97.5, 99.9)
PMB1256 (B03)		
Dose 2	61.1 (50.3, 71.2)	57.9 (47.3, 68.0)
Dose 3	92.5 (88.7, 95.3)	86.4 (81.8, 90.3)
PMB866 (B09)		
Dose 2	76.3 (66.4, 84.5)	65.3 (54.8, 74.7)
Dose 3	86.2 (81.6, 90.1)	77.0 (71.6, 81.9)
PMB431 (B15)		
Dose 2	96.8 (90.9, 99.3)	86.5 (78.0, 92.6)
Dose 3	98.2 (95.9, 99.4)	96.7 (93.9, 98.5)
PMB648 (B16)		
Dose 2	61.6 (50.5, 71.9)	51.6 (41.1, 62.0)
Dose 3	81.7 (76.6, 86.0)	78.0 (72.6, 82.8)
Proportion of subjects who achieved hSBA ≥ LLOQ (**LLOQ = hSBA titer 1:16)**		
PMB3010 (A06)		
Dose 2	84.0 (75.0, 90.8)	77.8 (67.8, 85.9)
Dose 3	95.7 (92.6, 97.8)	92.0 (88.1, 94.9)
PMB824 (A12)		
Dose 2	67.4 (57.0, 76.6)	57.6 (46.9, 67.9)
Dose 3	75.1 (69.6, 80.1)	71.3 (65.5, 76.5)
PMB1989 (A19)		
Dose 2	84.5 (75.8, 91.1)	87.4 (79.0, 93.3)
Dose 3	92.7 (89.0, 95.5)	95.8 (92.7, 97.8)

Abbreviations: fHBP = factor H binding protein; hSBA = serum bactericidal assay using human complement; LLOQ = lower limit of quantitation.

Note: LLOQ = 1:16 for A06, A12, and A19; 1:8 for A07, A15, A29, B03, B09, B15, and B16.

a The evaluable immunogenicity population and the post–Vaccination 2 per-protocol (evaluable immunogenicity) population were used for the evaluation at Dose 3 and Dose 2, respectively.

b Study B1971009 = NCT01830855 and Study B1971016 = NCT01352845.

c The denominators ranged from 86 to 97 after Dose 2 and 266 to 281 after Dose 3, depending on the strain.

d The denominators ranged from 90 to 96 after Dose 2 and 273 to 284 after Dose 3, depending on the strain.

Table 3. Immune Responses Among Individuals 10 to 25 Years of Age With a Defined hSBA Titer Against 10 Additional Strains (Study B1971009 and Study B1971016)[a,b]

e The strains expressing variants A06, A12, A19, A07, A15, A29, B03, B09, B15, and B16 correspond to strains PMB3010, PMB824, PMB1989, PMB3040, PMB1672, PMB3175, PMB1256, PMB866, PMB431, and PMB648, respectively.
f For the second and third doses, serum was obtained approximately 1 month after vaccination.
g Exact 2-sided confidence interval (Clopper and Pearson) based upon the observed proportion of subjects.

Concomitant vaccine administration

In Study B1971010 conducted in Europe, the immunogenicity of dTaP-IPV (a combined low-dose diphtheria, tetanus, acellular pertussis, and inactivated poliomyelitis virus vaccine) given concomitantly with the first dose of Trumenba was evaluated in adolescents 11 to <19 years of age. Noninferiority was demonstrated, as the lower limit of the 2-sided 95% CI for the difference in proportion of responders between the Trumenba + dTaP-IPV group (Group 1) and the dTaP-IPV–alone group (Group 2) 1 month after the dTaP-IPV dose was greater than -0.10 (-10%) for the 9 antigens in dTaP-IPV (ie, the lowest lower bound of the 95% CI on the proportion difference was -4.7% [pertussis toxoid]).

In Study B1971011 conducted in the United States, the immunogenicity of concomitantly administered Trumenba and HPV4 vaccine was evaluated in adolescents 11 to <18 years of age. Immune responses were evaluated by comparisons of geometric mean titers (GMTs) for each human papillomavirus (HPV) type at 1 month after the third HPV4 vaccination and hSBA GMTs using two meningococcal serogroup B test strains [variants A22 and B24] 1 month after the third vaccination with Trumenba. 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. One month after Dose 3 with HPV4, ≥ 99% of subjects seroconverted to all 4 HPV antigens in both the saline + HPV4 and Trumenba + HPV4 groups.

In Study B1971015 conducted in the United States, the immunogenicity of concomitantly administered Trumenba with quadrivalent meningococcal polysaccharide conjugate (MCV4) and Tdap vaccines was evaluated in adolescents 10 to <13 years of age. Immune responses were evaluated by comparisons of GMTs for each of 10 MCV4 and Tdap antigens 1 month after the first vaccination. The criterion for the noninferiority margin of 1.5-fold was met for all MCV4 and Tdap antigens.

Persistence of immunity

Study B1971005 conducted in Europe and Australia was a Phase 2, randomised, single-blind, placebo-controlled trial of the safety, immunogenicity, and tolerability of Trumenba at doses of 60 µg, 120 µg, and 200 µg (using a 0, 2, and 6-month schedule) in healthy adolescents 11 to 18 years old. The study was conducted in 2 stages. Stage 1 was designed to assess the safety and immunogenicity of Trumenba and to provide the basis for the dose-level selection. Stage 2 of the study was designed to evaluate the duration of the Trumenba-specific immune responses for up to 4 years after the third vaccination (Table 4).

Table 4. Persistence of the Immune Responses Among Individuals 11 to 18 Years of Age Administered Trumenba on a 0-, 2-, and 6-Month Schedule Achieving a Defined hSBA Titer (Study B1971005, Stage 2)[a,b]

fHBP (Variant)[e]	**Trumenba 120 µg[c]** **% (95% CI)[f]**	**Control[d]** **% (95% CI)[f]**
PMB80 (A22)		
Proportion of subjects who achieved hSBA ≥ LLOQ		
Before Dose 1	22.6 (16.5, 30.1)	24.4 (16.1, 35.1)
1 Month after Dose 3	95.3 (90.5, 97.8)	28.8 (19.9, 39.6)
6 Months 1 week after last dose in Stage 1	60.2 (52.5, 67.5)	20.3 (12.8, 30.5)
12 Months after last dose in Stage 1	54.2 (46.3, 61.9)	28.9 (19.9, 40.1)
24 Months after last dose in Stage 1	53.6 (45.7, 61.3)	31.1 (21.6, 42.5)
48 Months after last dose in Stage 1	59.0 (50.4, 67.0)	34.3 (24.0, 46.4)
PMB2001 (A56)		
Proportion of subjects who achieved hSBA ≥ LLOQ		
Before Dose 1	22.7 (12.7, 37.3)	23.8 (10.3, 46.0)
1 Month after Dose 3	100.0 (85.5, 99.9)	34.8 (18.4, 55.7)
6 Months 1 week after last dose in Stage 1	89.4 (76.9, 95.5)	21.7 (9.3, 42.8)
12 Months after last dose in Stage 1	68.8 (54.4, 80.2)	26.1 (12.2, 47.2)
24 Months after last dose in Stage 1	53.1 (39.2, 66.5)	36.4 (19.3, 57.7)
48 Months after last dose in Stage 1	51.1 (37.1, 64.9)	34.8 (18.4, 55.7)
PMB2948 (B24)		
Proportion of subjects who achieved hSBA ≥ LLOQ		
Before Dose 1	8.8 (5.2, 14.5)	8.8 (4.2, 17.2)
1 Month after Dose 3	93.3 (88.0, 96.4)	15.2 (8.8, 24.9)
6 Months 1 week after last dose in Stage 1	57.1 (49.3, 64.4)	13.8 (7.8, 23.1)
12 Months after last dose in Stage 1	54.7 (46.6, 62.4)	12.8 (7.0, 22.2)
24 Months after last dose in Stage 1	53.9 (46.0, 61.7)	16.2 (9.4, 26.4)
48 Months after last dose in Stage 1	57.0 (48.3, 65.3)	23.5 (14.9, 35.0)
PMB2707 (B44)		

Table 4. Persistence of the Immune Responses Among Individuals 11 to 18 Years of Age Administered Trumenba on a 0-, 2-, and 6-Month Schedule Achieving a Defined hSBA Titer (Study B1971005, Stage 2)[a,b]		
Proportion of subjects who achieved hSBA ≥ LLOQ		
Before Dose 1	2.0 (0.3, 13.1)	0.0 (0.0, 24.7)
1 Month after Dose 3	95.7 (84.5, 98.9)	0.0 (0.0, 24.7)
6 Months 1 week after last dose in Stage 1	36.7 (24.5, 50.9)	0.0 (0.0, 24.7)
12 Months after last dose in Stage 1	29.2 (18.1, 43.4)	4.0 (0.6, 23.5)
24 Months after last dose in Stage 1	22.4 (12.9, 36.2)	4.0 (0.6, 23.5)
48 Months after last dose in Stage 1	20.4 (11.3, 33.9)	12.0 (3.9, 31.3)

Abbreviations: fHBP = factor H binding protein; hSBA = serum bactericidal assay using human complement; LLOQ = lower limit of quantitation.
Note: All testing was performed with the validated hSBA.
Note: Testing using the validated assay for variants A56 and B44 was only done for a subset of 75 subjects (25 subjects from the control group and 50 subjects from the Trumenba 120-µg group).
Note: LLOQ = 1:16 for A22; 1:8 for A56, B24, and B44.
Note: For all Stage 2 subjects, the last dose in Stage 1 was Dose 3.
a. Intent-to-treat population.
b. Study B1971005 = NCT 00808028.
c. The denominators ranged from 44 to 163 depending on the strain.
d. The denominators ranged from 21 to 80 depending on the strain.
e. The strains expressing variants A22, A56, B24, and B44 correspond to strains PMB80, PMB2001, PMB2948, and PMB2707, respectively.
f. Confidence intervals (CIs) are based on a generalized linear model with vaccine group and sampling time as fixed effects and a logit function.

INDICATIONS

Trumenba is indicated in individuals 10 years and older for active immunisation to prevent invasive meningococcal disease caused by *Neisseria meningitidis* serogroup B.

CONTRAINDICATIONS

- Hypersensitivity to the active substances or to any of the excipients contained in the vaccine.(see DESCRIPTION, Excipients)

- Severe allergic reaction (e.g., anaphylaxis) after any previous dose of Trumenba or to any component of this vaccine.

PRECAUTIONS

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of the vaccine.

Do not inject intravenously, intradermally, or subcutaneously.

As with any intramuscular vaccine, Trumenba should be given with caution to individuals with thrombocytopenia or any coagulation disorder or to those receiving anticoagulant therapy, unless the potential benefit clearly outweighs the risk of administration.

There are no data on the use of Trumenba in immunocompromised individuals. Immunocompromised individuals, including individuals receiving immunosuppressant therapy, may have a diminished immune response to Trumenba.

As with any vaccine, vaccination with Trumenba may not protect all vaccine recipients.

Paediatric population

The safety and efficacy of Trumenba in children below the age of 10 years of age has not been established. In a clinical study, 90% of infants less than 12 months of age who were vaccinated with a reduced dosage formulation had fever.

Elderly population

Trumenba has not been studied in adults older than 65 years of age.

Effects on Fertility

Rabbits given 4 x 200 μg doses of Trumenba (2-week intervals between doses) did not show harmful effects with respect to fertility in females. Trumenba has not been evaluated for impairment of fertility in males.

Use in Pregnancy (Category B1)

Reproduction studies performed in female rabbits given 4 x 200 μg doses of Trumenba (2-week intervals between doses) revealed no evidence of harm to the fetus.

There are no data from the use of Trumenba vaccine in pregnant women and because animal reproductive studies are not always predictive of the human response, this vaccine should be used during pregnancy only if clearly needed.

Use in Lactation

It is unknown whether Trumenba is excreted in human milk.

Trumenba should only be used during breast-feeding when the possible advantages outweigh the potential risks.

Genotoxicity

Trumenba has not been evaluated for genotoxic potential.

Carcinogenicity

Trumenba has not been evaluated for carcinogenic potential.

Effects on ability to drive and use machines

Trumenba has no or negligible influence on the ability to drive and use machines.

INTERACTIONS WITH OTHER MEDICINES

Trumenba can be given concomitantly with any of the following vaccines: Reduced Diphtheria Toxoid, Tetanus Toxoid, Acellular Pertussis and Inactivated Poliovirus Vaccine (dTaP-IPV), Quadrivalent Human Papillomavirus vaccine (HPV4), Meningococcal Serogroups A, C, Y, W conjugate vaccine (MnACWY) and Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap).

Do not mix Trumenba with other vaccines or products in the same syringe.

Individuals with impaired immune responsiveness due to the use of immunosuppressive therapy (including irradiation, corticosteroids, antimetabolites, alkylating agents, and cytotoxic agents) may not respond optimally to active immunisation with Trumenba.

ADVERSE EFFECTS

The safety of Trumenba was investigated in 11 completed clinical studies that enrolled a total of 20,803 subjects, of which 15,294 subjects received at least one dose of Trumenba administered alone or concomitantly with a licensed vaccine and 5509 control subjects received either saline alone, a licensed vaccine alone, or saline and a licensed vaccine.

Adverse events and adverse reactions reported in clinical trials are presented as tabulated summaries below.

Adverse events during the vaccination phase are reported in Table 5. These exclude reactogenicity events reported within 7 days of vaccination.

Adverse reactions are reported in Table 6.

Table 5. Adverse Events Excluding Reactogenicity Events Reported During the Vaccination Phase (Reported by 1% or More Subjects) – Subjects Who Received at Least 1 Dose of Bivalent rLP2086 Final Formulation (120 µg Dose Level) on a 0-, 2-, and 6-Month Schedule – Core Studies Pooled

System Organ Class Preferred Term	rLP2086[a] (N=13284) n (%)	Control[b] (N=5509) n (%)
Any event	5000 (37.64)	2159 (39.19)
Gastrointestinal disorders	651 (4.90)	285 (5.17)
Nausea	167 (1.26)	55 (1.00)
General disorders and administration site conditions	406 (3.06)	145 (2.63)
Pyrexia	133 (1.00)	56 (1.02)
Infections and infestations	3023 (22.76)	1314 (23.85)
Upper respiratory tract infection	659 (4.96)	291 (5.28)

Table 5. Adverse Events Excluding Reactogenicity Events Reported During the Vaccination Phase (Reported by 1% or More Subjects) – Subjects Who Received at Least 1 Dose of Bivalent rLP2086 Final Formulation (120 µg Dose Level) on a 0-, 2-, and 6-Month Schedule – Core Studies Pooled

System Organ Class Preferred Term	rLP2086[a] (N=13284) n (%)	Control[b] (N=5509) n (%)
Nasopharyngitis	448 (3.37)	208 (3.78)
Pharyngitis	326 (2.45)	131 (2.38)
Gastroenteritis	242 (1.82)	108 (1.96)
Sinusitis	196 (1.48)	74 (1.34)
Pharyngitis streptococcal	147 (1.11)	68 (1.23)
Bronchitis	130 (0.98)	75 (1.36)
Injury, poisoning and procedural complications	829 (6.24)	350 (6.35)
Ligament sprain	164 (1.23)	66 (1.20)
Fall	145 (1.09)	54 (0.98)
Musculoskeletal and connective tissue disorders	523 (3.94)	214 (3.88)
Nervous system disorders	535 (4.03)	233 (4.23)
Headache	263 (1.98)	141 (2.56)
Psychiatric disorders	183 (1.38)	81 (1.47)
Respiratory, thoracic and mediastinal disorders	654 (4.92)	262 (4.76)
Cough	193 (1.45)	84 (1.52)
Oropharyngeal pain	174 (1.31)	71 (1.29)
Skin and subcutaneous tissue disorders	422 (3.18)	171 (3.10)

Note: Studies B1971004, B1971005, B1971009, B1971010, B1971011, B1971014, B1971015, and B1971016 are summarised in this table.

a. The rLP2086 arm from B1971009 combined Group 1 (Lot 1), Group 2 (Lot 2), and Group 3 (Lot 3); the rLP2086 arm from B1971010 received Repevax at Month 0 in addition to rLP2086 at Months 0, 2, and 6; the rLP2086 arm from B1971011 combined Group 1 (both Gardasil and rLP2086 at Months 0, 2, and 6) and Group 2 (both saline and rLP2086 at Months 0, 2, and 6); the rLP2086 arm from B1971015 combined Group 1 (MCV4 and Tdap at Month 0 in addition to rLP2086 at Months 0, 2, and 6) and Group 3 (saline at Month 0 in addition to rLP2086 at Months 0, 2, and 6).

b. The control arm from B1971004 received Tdap at Month 0 and saline at Months 2 and 6; the control arm from B1971010 received Repevax at Month 0 and saline at Months 0, 2, and 6; the control arm from B1971011 received Gardasil and saline at Months 0, 2, and 6; the control arm from B1971015 received MCV4, Tdap, and saline at Month 0 and saline at Months 2 and 6; the control arm from B1971009 and B1971014 received HAV vaccine at Months 0 and 6 and saline at Month 2.

Table 6. Percentages of Subjects 10 to 18 Years of Age (B1971009) and 18 to 25 Years of Age (B1971016) Reporting Local and Systemic Adverse Reactions Within 7 Days After Any Vaccination

	B1971009		B1971016	
	rLP2086 (Lots 1-3)	HAV/Saline	rLP2086	Saline
Local Reactions/Systemic Events	N[a]=2686	N[a]=893	N[a]=2438	N[a]=808
	%	%	%	%
Pain at injection site	92.6	58.8	89.6	18.2
Redness at injection site	24.1	2.4	22.0	1.0
Swelling at injection site	27.4	2.9	25.1	1.0
Fever (≥38.0°C)[b, c, d]	9.8	5.2	4.4	1.7
Vomiting	6.9	4.6	5.3	4.6
Diarrhea	19.5	20.9	20.4	19.6
Headache	67.1	53.4	59.1	48.4
Fatigue	65.5	50.8	64.6	50.9
Chills	36.3	25.4	28.6	16.5
Muscle pain	37.7	28.4	37.6	21.0
Joint pain	33.2	23.4	29.7	16.8

a. N = number of subjects with known values after any vaccination.
b. Denominator for B1971009 HAV/Saline is 892.
c. Denominator for B1971016 rLP2086 is 2432.
d. Denominator for B1971016 Saline is 807.

Nausea is a systemic adverse reaction that was actively collected within 7 days of vaccination in early phase studies. In a study of adolescents 11-18 years of age (Study B1971005 Stage 1), nausea was reported in 23.7% of subjects (n=198) receiving Trumenba and 14.2% of subjects (n=120) who received control.

Adverse reactions from Trumenba post-marketing experience

The following is considered an adverse reaction for Trumenba and was reported in the post-marketing experience. Because this reaction was derived from spontaneous reports, the frequency could not be determined.

Immune system disorder: Allergic reactions

DOSAGE AND ADMINISTRATION

The vaccine should be shaken vigorously to ensure that a homogeneous white suspension is obtained. Do not use the vaccine if it cannot be re-suspended.

The vaccine should be visually inspected for particulate matter and discoloration prior to administration. This product should not be used if particulate matter or discoloration is found.

Dosage

Standard schedule for routine immunisation: 2 doses (0.5 ml each) administered at 0 and 6 months.

Schedule for individuals at increased risk of invasive meningococcal disease: 2 doses (0.5 ml each) administered at least 1 month apart, followed by a third dose at least 4 months after the second dose.

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

Method of administration

For intramuscular injection only. The preferred site for injection is the deltoid muscle of the upper arm.

Separate injection sites and different syringes must be used if more than one vaccine is administered at the same time.

Each pre-filled syringe is for single use in one patient only. Discard any residue.

Trumenba is not interchangeable with other meningococcal group B vaccines due to different vaccine compositions, age indications and dosing schedules.

Incompatibilities

Do not mix Trumenba with other vaccines or products in the same syringe.

OVERDOSAGE

Experience of overdose is limited. Overdose with Trumenba is unlikely because it is provided in a prefilled syringe.

In the event of overdose, monitoring of vital functions and possible symptomatic treatment is recommended.

For information on the management of overdose, contact the Poison Information Centre on 131126 (Australia).

PRESENTATION AND STORAGE CONDITIONS

Presentation

Trumenba is supplied as a 0.5 mL white suspension for injection, provided in a pre-filled syringe (Type I glass) containing *Neisseria meningitidis* serogroup B recombinant lipidated-

factor H binding protein subfamily A 60 µg

factor H binding protein subfamily B 60 µg

All syringe components are latex-free.

Pack sizes of 1 and 10* prefilled syringes, with* or without needle.

Not commercially available*

Storage Conditions

Store in a refrigerator (2°C-8°C).

Syringes should be stored in the refrigerator horizontally to minimize the re-dispersion time.

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

NAME AND ADDRESS OF THE SPONSOR

Pfizer Australia Pty Ltd
38 – 42 Wharf Road
West Ryde NSW 2114

POISON SCHEDULE OF THE MEDICINE

Schedule 4 – Prescription Only Medicine

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (THE ARTG)

14 September 2017

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