

AUSTRALIAN PRODUCT INFORMATION - TRUMENBA[®] (Meningococcal group B vaccine) suspension for injection pre-filled syringe

1. NAME OF THE MEDICINE

Meningococcal group B vaccine.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

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).

Excipient(s) with known effect:

- Sodium

For the full list of excipients, see Section 6.1 - List of excipients.

3. PHARMACEUTICAL FORM

Suspension for injection pre-filled syringe.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

4.2 Dose and method of 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.

4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients contained in the vaccine.(see Section 6.1 – List of Excipients)
- Severe allergic reaction (e.g., anaphylaxis) after any previous dose of Trumenba or to any component of this vaccine.

4.4 Special warnings and precautions for use

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 other injectable vaccines, syncope (fainting) can occur in association with administration of Trumenba. Procedures should be in place to avoid injury from fainting.

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.

Persons with certain complement deficiencies and persons receiving treatment that inhibits terminal complement activation (for example, eculizumab) are at increased risk for invasive

disease caused by *Neisseria meningitidis* serogroup B even if they develop antibodies following vaccination with Trumenba.

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

Use in the elderly

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

Paediatric use

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.

Effects on laboratory tests

No data available.

4.5 Interactions with other medicines and other forms of interactions

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.

4.6 Fertility, pregnancy and lactation

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 – 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.

4.7 Effects on ability to drive and use machines

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

4.8 Adverse effects (undesirable 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 (aged 10 years and older) 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. The most common adverse reactions observed were injection site pain, redness and swelling at the vaccination site, headache, fatigue, chills, diarrhoea, muscle pain, joint pain and nausea.

Adverse reactions reported in clinical studies are listed in this section per system organ class, in decreasing order of frequency and seriousness. The frequency is defined as follows: very common ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$), uncommon ($\geq 1/1,000$ to $< 1/100$), rare ($\geq 1/10,000$ to $< 1/1,000$), very rare ($< 1/10,000$), not known (cannot be estimated from available data).

Nervous system disorders

Very Common: Headache

Gastrointestinal disorders

Very Common: Diarrhoea; nausea

Common: Vomiting

Musculoskeletal and connective tissue disorders

Very Common: Myalgia; arthralgia

General disorders and administration site conditions

Very Common: Chills; fatigue; erythema, swelling and pain at injection site

Common: Pyrexia ($\geq 38^{\circ}\text{C}$)

Table 1 below presents the percentages of subjects reporting local and systemic adverse reactions within 7 days after any vaccination in the two pivotal Phase 3 studies.

Table 1. 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

Local Reactions/Systemic Events	B1971009		B1971016	
	rLP2086 (Lots 1-3) N ^a =2686	HAV/Saline N ^a =893	rLP2086 N ^a =2438	Saline 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 ($\geq 38.0^{\circ}\text{C}$) ^{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.

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 disorders: Allergic reactions

Nervous system disorders: Syncope (fainting)

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 Overdose

Signs and symptoms

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

Recommended treatment

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

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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 Immunogenicity below). 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 2.

Table 2. Immune Responses Among Individuals 11 to 18 Years of Age Administered Trumenba After Various 2- and 3-Dose Schedules (Study B1971012)^{a,b}					
fHBP Variant^{h,i}	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
	%/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 \geq 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 \geq 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 \geq LLOQ for all 4 hSBA strains combined) ^{ik}						
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)	--	--	--	
<p>Abbreviations: fHBP = factor H binding protein; GMT = geometric mean titer; hSBA = serum bactericidal assay using human complement; LLOQ = lower limit of quantitation.</p> <p>Note: LLOQ = 1:16 for PMB80 (A22) and 1:8 for PMB2001 (A56), PMB2948 (B24), and PMB2707 (B44).</p> <p>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 $\geq 1:16$. (2) For subjects with a baseline hSBA titer $\geq 1:4$, a 4-fold response was defined as an hSBA titer ≥ 4 times the LLOQ or ≥ 4 times the baseline titer, whichever was higher.</p> <p>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.</p> <p>b NCT01299480.</p> <p>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.</p> <p>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.</p> <p>e Group 3 (0 and 6 months). The denominators ranged from 188 to 203 after Dose 2.</p> <p>f Group 4 (0 and 2 months). The denominators ranged from 161 to 171 after Dose 2.</p> <p>g Group 5 (0 and 4 months). The denominators ranged from 78 to 81 after Dose 2.</p> <p>h The strains expressing variants A22, A56, B24, and B44 correspond to strains PMB80, PMB2001, PMB2948, and PMB2707, respectively.</p> <p>i For the second and third doses, serum was obtained approximately 1 month after vaccination.</p> <p>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.</p> <p>k Composite response = hSBA \geq LLOQ for all 4 primary meningococcal B strains combined.</p>						

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 3.

Table 3. 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}		
hBP Variant^{f,g}	Study B1971009 Aged 10 to 18 Years	Study B1971016 Aged 18 to 25 Years
	%/GMT^e (95% CI)^h	%/GMT^e (95% CI)^h
PMB80 (A22)		
	Proportion of subjects who achieved \geq 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 \geq 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 \geq 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 \geq 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 \geq 1:16 or the LLOQ (whichever titer is higher). (2) For subjects with a baseline hSBA titer \geq LOD and < LLOQ, a response is defined as an hSBA titer \geq 4 times the LLOQ. (3) For subjects with a baseline hSBA titer \geq LLOQ, a response is defined as an hSBA titer \geq 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 \geq 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 4).

fHBP Variant ^{e,f}	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	
	(% (95% CI) ^g		(% (95% CI) ^g	
Proportion of subjects who achieved hSBA \geq LLOQ (LLOQ = hSBA titer 1:8)				
PMB3040 (A07)				
Dose 2	93.8 (86.9, 97.7)		97.9 (92.6, 99.7)	
Dose 3	96.4		95.7	

Table 4. 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}

	(93.5, 98.3)	(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 \geq 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.

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 5).

fHBP (Variant) ^e	Trumenba 120 µg ^c	Control ^d
	% (95% CI) ^f	% (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	28.8

Table 5. 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}

	(90.5, 97.8)	(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 \geq 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 \geq 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)		
Proportion of subjects who achieved hSBA \geq 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- μ g 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.		

Table 5. 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}

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.

5.2 Pharmacokinetic properties

No data available.

5.3 Preclinical safety data

Genotoxicity

Trumenba has not been evaluated for genotoxic potential.

Carcinogenicity

Trumenba has not been evaluated for carcinogenic potential.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride,
Histidine,
Water for injections,
Aluminium phosphate,
Polysorbate 80.

6.2 Incompatibilities

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

6.3 Shelf life

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 Special precautions for storage

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.

6.5 Nature and contents of container

Trumenba is supplied as a 0.5 mL white suspension for injection, provided in a pre-filled syringe (Type I glass).

All syringe components are latex-free.

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

Not commercially available*

6.6 Special precautions for disposal

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements

6.7 Physicochemical properties

Chemical structure

No data available.

CAS number

No data available.

7. MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 4 – Prescription Only Medicine

8. SPONSOR

Pfizer Australia Pty Ltd
Level 17, 151 Clarence Street
Sydney NSW 2000
Toll Free Number: 1800 675 229
www.pfizer.com.au

9. DATE OF FIRST APPROVAL

14 September 2017

10. DATE OF REVISION

13 February 2019

® Registered trademark

Summary Table of Changes

Section changed	Summary of new information
Section 8	Sponsor address amended to reflect new address.