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 discolouration prior to administration. This product should not be used if particulate matter or discolouration is found.

Dosage

Standard two-dose schedule for routine immunisation: administer 0.5 mL at 0 and 6 months.

Three-dose schedule for individuals at increased risk of invasive meningococcal disease: administer 2 doses of 0.5 mL 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.

A booster dose should be considered following either dosing regimen for individuals at continued risk of invasive meningococcal disease (see section 5.1 Pharmacodynamic properties).

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 serogroup 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 (MenACWY) 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 foetus.

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 over 23,000 subjects, of which approximately 17,000 subjects received at least one dose of Trumenba administered alone or concomitantly with a licensed vaccine and over 6,000 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 (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000), very rare (< 1/10,000), not known (cannot be estimated from available data).

Adverse reactions following booster vaccination in 301 subjects aged 15 to 23 years were similar to adverse reactions during the primary Trumenba vaccination series approximately 4 years earlier.

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 (≥ 38°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

	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.

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

Pharmacotherapeutic group: Vaccines

ATC code: J07AH09 Meningococcus B, multicomponent vaccine

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 serogroup 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 response (hSBA titre of at least 1:8 or 1:16 depending on the hSBA strain), the proportions of subjects with a 4-fold or greater increase from baseline in hSBA titre for each of the four strains and the composite response (a response for the four hSBA strains combined). The studies also assessed the proportion of subjects achieving a defined hSBA titre against a panel of 10 additional strains, each

expressing a different fHbp variant. These additional hSBAs support and extend the breadth of vaccine coverage demonstrated by the 4 representative primary strains.

Immunogenicity

The immunogenicity of Trumenba described in this section is based on results from in four clinical studies:

- Following the two-dose schedule (0 and 6 months) in subjects 10 to 25 years of age in the United States (US) and Europe (Study B1971057).
- Following the three-dose schedule (0, 2, and 6 months) in subjects 10 to 25 years of age globally (Studies B1971009 and B1971016).
- Following the two-dose (0 and 6 months) and three-dose schedules (0, 1-2, and 6 months) in subjects 11 to 18 years of age in Europe (Study B1971012).

Study B1971057 is a Phase 3, randomised, active-controlled, observer-blinded, multi-center trial in which subjects received Trumenba at 0 and 6 months (Trumenba was co-administered with MenACWY-CRM for the first dose) or an investigational pentavalent meningococcal vaccine at 0 and 6 months. The hSBA responses to four test strains observed after the second dose of Trumenba are presented in Table 2.

Table 2. Immune Responses Among Subjects 10 to 25 Years of Age 1 Month Following the Second Dose of Trumenba Given on a 0- and 6-Month Schedule (Study B1971057)[a, b,]

hSBA Strain (fHbp Variant)[c]		**N**	**% (95% CI)[d]**
PMB80 (A22)	**% hSBA ≥ 1:16**		
		852	91.0 (88.8, 92.8)
	≥ 4-Fold rise in hSBA titre (%)		
		827	73.8 (70.6, 76.7)
	hSBA GMT		
	Before Dose 1	839	10.7 (10.3, 11.1)
	Dose 2	852	49.3 (46.2, 52.6)
PMB2001 (A56)	**% hSBA ≥ 1:8**		
		854	99.4 (98.6, 99.8)
	≥ 4-Fold rise in hSBA titre (%)		
		823	95.0 (93.3, 96.4)
	hSBA GMT		
	Before Dose 1	833	5.3 (5.0, 5.6)
	Dose 2	854	139.5 (130.6, 149.1)
PMB2948 (B24)	**% hSBA ≥ 1:8**		
		842	79.3 (76.4, 82.0)
	≥ 4-Fold rise in hSBA titre (%)		
		835	67.4 (64.1, 70.6)
	hSBA GMT		

Table 2. Immune Responses Among Subjects 10 to 25 Years of Age 1 Month Following the Second Dose of Trumenba Given on a 0- and 6-Month Schedule (Study B1971057)[a, b,]			
hSBA Strain (fHbp Variant)[c]		**N**	**% (95% CI)[d]**
	Before Dose 1	855	4.9 (4.7, 5.1)
	Dose 2	842	21.2 (19.6, 22.9)
PMB2707 (B44)	**% hSBA ≥ 1:8**		
		853	94.5 (92.7, 95.9)
	≥ 4-Fold rise in hSBA titre (%)		
		850	86.4 (83.9, 88.6)
	hSBA GMT		
	Before Dose 1	861	4.3 (4.2, 4.5)
	Dose 2	853	37.8 (35.1, 40.8)
Composite response[e]			
	Before Dose 1	799	1.8 (1.0, 2.9)
	Dose 2	814	74.3 (71.2, 77.3)

Abbreviations: fHbp = factor H binding protein; GMT = geometric mean titre; hSBA = serum bactericidal assay using human complement; LLOQ = lower limit of quantitation; LOD = limit of detection.
Note: The LLOQ is an hSBA titre = 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 titre <1:4 (LOD), a 4-fold response was defined as an hSBA titre ≥1:16. (2) For subjects with a baseline hSBA titre ≥ LOD and < LLOQ, a response is defined as an hSBA titre ≥4 times the LLOQ. (3) For subjects with a baseline hSBA titre ≥ LLOQ, a response is defined as an hSBA titre ≥4 times the baseline titre.
a Evaluable immunogenicity population.
b NCT03135834.
c For the second dose, serum was obtained approximately 1 month after vaccination.
d Exact 2-sided confidence interval (Clopper-Pearson method) based upon the observed proportion of subjects. For GMTs, CIs are obtained by exponentiating the limits of CIs for the mean logarithm of the hSBA titres (based on the Student t distribution).
e Composite response = hSBA ≥ LLOQ for all 4 primary meningococcal B strains.

The proportion of subjects achieving a defined hSBA titre after 2 doses of Trumenba, administered on a 0- 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 Subjects 10 to 25 Years of Age Against 10 Additional Strains 1 Month Following the Second Dose of Trumenba Given on a 0- and 6-Month Schedule (Study B1971057)[a,b]		
hSBA Strain (fHbp Variant)[c]	**N**	**% (95% CI)[d]**
% hSBA ≥1:8		
PMB3040 (A07)	157	96.8 (92.7, 99.0)
PMB1672 (A15)	165	89.1 (83.3, 93.4)
PMB3175 (A29)	166	95.2 (90.7, 97.9)

Table 3. Immune Responses Among Subjects 10 to 25 Years of Age Against 10 Additional Strains 1 Month Following the Second Dose of Trumenba Given on a 0- and 6-Month Schedule (Study B1971057)[a,b]		
hSBA Strain (fHbp Variant)[c]	**N**	**% (95% CI)[d]**
PMB1256 (B03)	164	74.4 (67.0, 80.9)
PMB866 (B09)	166	71.1 (63.6, 77.8)
PMB431 (B15)	167	85.0 (78.7, 90.1)
PMB648 (B16)	164	77.4 (70.3, 83.6)
% hSBA ≥ 1:16		
PMB3010 (A06)	159	89.3 (83.4, 93.6)
PMB824 (A12)	157	83.4 (76.7, 88.9)
PMB1989 (A19)	167	90.4 (84.9, 94.4)

Abbreviations: fHbp=factor H binding protein; hSBA=serum bactericidal assay using human complement; LLOQ = lower limit of quantitation.
Note: The LLOQ is an hSBA titre = 1:16 for A06, A12, and A19; 1:8 for A07, A15, A29, B03, B09, B15, and B16.
a Evaluable immunogenicity population.
b NCT03135834.
c For second dose, serum was obtained approximately 1 month after vaccination.
d Exact 2-sided confidence interval (Clopper and Pearson) based upon the observed proportion of subjects.

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 (Group 4). The study assessed the safety, tolerability, immunogenicity, and demonstration of 3 lots of Trumenba administered on a 0-, 2-, and 6-month schedule. The hSBA responses to four test strains observed after the third dose in Group 1 and 4 are presented in Table 4. 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 to four test strains observed after the third dose in Group 1 and 2 are presented in Table 4.

Table 4. Immune Responses Among Subjects 10 to 25 Years of Age 1 Month Following the Third Dose of Trumenba or Control Given on a 0-, 2-, and 6-Month Schedule (Study B1971009 and Study B1971016)[a,b]

		Study B1971009 (10-18 years of age)				Study B1971016 (18-25 years of age)			
		Group 1		Group 4		Group 1		Group 2	
		Trumenba		HAV/saline		Trumenba		Saline	
hSBA Strain (fHbp Variant)[c]		**N**	**% (95% CI)[d]**	**N**	**% (95% CI)[d]**	**N**	**% (95% CI)[d]**	**N**	**% (95% CI)[d]**
PMB80 (A22)	**% hSBA ≥ 1:16**								
		1266	97.8 (96.8, 98.5)	749	34.0 (30.7, 37.6)	1714	93.5 (92.2, 94.6)	577	36.6 (32.6, 40.6)
	≥ 4-Fold rise in hSBA titre (%)								
		1225	83.2 (81.0, 85.2)	730	9.6 (7.6, 12.0)	1695	80.5 (78.6, 82.4)	568	6.3 (4.5, 8.7)
	hSBA GMT								
	Before Dose 1	1238	12.6 (12.1 13.1)	748	13.4 (12.6, 14.1)	1704	12.8 (12.3, 13.3)	573	13.0 (12.2, 13.9)
	Dose 3	1266	86.8 (82.3, 91.5)	749	12.6 (12.0, 13.4)	1714	74.3 (70.2, 78.6)	577	13.2 (12.4, 14.1)
PMB2001 (A56)	**% hSBA ≥ 1:8**								
		1229	99.5 (98.9, 99.8)	363	27.5 (23.0, 32.5)	1708	99.4 (98.9, 99.7)	552	34.2 (30.3, 38.4)
	≥ 4-Fold rise in hSBA titre (%)								
		1128	90.2 (88.4, 91.9)	337	11.3 (8.1, 15.1)	1642	90.0 (88.4, 91.4)	533	10.3 (7.9, 13.2)
	hSBA GMT								
	Before Dose 1	1135	8.4 (7.8, 9.1)	362	8.3 (7.2, 9.5)	1657	8.8 (8.3, 9.3)	563	9.2 (8.3, 10.3)
	Dose 3	1229	222.5 (210.1, 235.6)	363	8.8 (7.6, 10.1)	1708	176.7 (167.8, 186.1)	552	9.1 (8.2, 10.1)
PMB2948 (B24)	**% hSBA ≥ 1:8**								
		1250	87.1 (85.1, 88.9)	762	7.0 (5.3, 9.0)	1702	95.1 (93.9, 96.0)	573	30.2 (26.5, 34.1)
	≥ 4-Fold rise in hSBA titre (%)								
		1235	79.8 (77.4, 82.0)	752	2.7 (1.6, 4.1)	1675	79.3 (77.3, 81.2)	562	5.5 (3.8, 7.7)
	hSBA GMT								
	Before Dose 1	1264	4.5 (4.4, 4.6)	758	4.6 (4.4, 4.8)	1696	7.6 (7.3, 8.0)	570	7.6 (7.0, 8.3)
	Dose 3	1250	24.1 (22.7, 25.5)	762	4.5 (4.4, 4.7)	1702	49.5 (46.8, 52.4)	573	7.2 (6.6, 7.8)
PMB2707 (B44)	**% hSBA ≥ 1:8**								
		1210	89.3 (87.4, 90.9)	393	5.3 (3.3, 8.1)	1703	87.4 (85.8, 89.0)	577	11.4 (9.0, 14.3)
	≥ 4-Fold rise in hSBA titre (%)								
		1203	85.9 (83.8, 87.8)	391	1.0 (0.3, 2.6)	1696	79.6 (77.6, 81.5)	573	1.6 (0.7, 3.0)
	hSBA GMT								
	Before Dose 1	1230	4.3 (4.2, 4.3)	391	4.3 (4.2, 4.5)	1716	4.8 (4.7, 4.9)	578	4.8 (4.6, 5.1)

Table 4. Immune Responses Among Subjects 10 to 25 Years of Age 1 Month Following the Third Dose of Trumenba or Control Given on a 0-, 2-, and 6-Month Schedule (Study B1971009 and Study B1971016)[a,b]

		Study B1971009 (10-18 years of age)				Study B1971016 (18-25 years of age)			
		Group 1		Group 4		Group 1		Group 2	
		Trumenba		HAV/saline		Trumenba		Saline	
hSBA Strain (fHbp Variant)[c]		**N**	**% (95% CI)[d]**	**N**	**% (95% CI)[d]**	**N**	**% (95% CI)[d]**	**N**	**% (95% CI)[d]**
	Dose 3	1210	50.9 (47.0, 55.2)	393	4.4 (4.2, 4.6)	1703	47.6 (44.2, 51.3)	577	4.8 (4.6, 5.1)
Composite response[e]									
	Before Dose 1	1088	1.1 (0.6, 1.9)	354	2.0 (0.8, 4.0)	1612	7.3 (6.0, 8.6)	541	6.1 (4.2, 8.5)
	Dose 3	1170	83.5 (81.3, 85.6)	353	2.8 (1.4, 5.1)	1664	84.9 (83.1, 86.6)	535	7.5 (5.4, 10.0)

Abbreviations: fHbp=factor H binding protein; GMT = geometric mean titre; hSBA=serum bactericidal assay using human complement; LLOQ = lower limit of quantitation; LOD = limit of detection.
Note: The LLOQ is an hSBA titre = 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 titre <1:4 (LOD), a 4-fold response was defined as an hSBA titre ≥1:16. (2) For subjects with a baseline hSBA titre ≥ LOD and < LLOQ, a response is defined as an hSBA titre ≥4 times the LLOQ. (3) For subjects with a baseline hSBA titre ≥ LLOQ, a response is defined as an hSBA titre ≥4 times the baseline titre.
a Evaluable immunogenicity population.
b Study 1009 = NCT01830855 and Study 1016 = NCT01352845.
c For the third dose, serum was obtained approximately 1 month after vaccination.
d Exact 2-sided confidence interval (Clopper-Pearson method) based upon the observed proportion of subjects. For GMTs, CIs are obtained by exponentiating the limits of CIs for the mean logarithm of the hSBA titres (based on the Student t distribution).
e Composite response = hSBA ≥ LLOQ for all 4 primary meningococcal B strains.

In Studies B1971009 and B1971016, the proportion of subjects achieving a defined hSBA titre after 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 5).

Table 5. Immune Responses Among Subjects 10 to 25 Years of Age Against 10 Additional Strains 1 Month Following the Third Dose of Trumenba Given on a 0-, 2-, and 6-Month Schedule (Study B1971009 and Study B1971016)[a,b]

hSBA Strain (fHbp Variant)[c]	Study B1971009 (10 to 18 Years of Age)		Study B1971016 (18 to 25 Years of Age)	
	N	**% (95% CI)[d]**	**N**	**% (95% CI)[d]**
% hSBA ≥1:8				
PMB3040 (A07)	280	96.4 (93.5, 98.3)	277	95.7 (92.6, 97.7)
PMB1672 (A15)	266	87.2 (82.6, 91.0)	279	91.8 (87.9, 94.7)
PMB3175 (A29)	278	98.6 (96.4, 99.6)	283	99.3 (97.5, 99.9)
PMB1256 (B03)	279	92.5 (88.7, 95.3)	273	86.4 (81.8, 90.3)
PMB866 (B09)	276	86.2 (81.6, 90.1)	274	77.0 (71.6, 81.9)
PMB431 (B15)	281	98.2 (95.9, 99.4)	276	96.7 (93.9, 98.5)

Table 5. Immune Responses Among Subjects 10 to 25 Years of Age Against 10 Additional Strains 1 Month Following the Third Dose of Trumenba Given on a 0-, 2-, and 6-Month Schedule (Study B1971009 and Study B1971016)[a,b]				
hSBA Strain (fHbp Variant)[c]	**Study B1971009 (10 to 18 Years of Age)**		**Study B1971016 (18 to 25 Years of Age)**	
	N	**% (95% CI)[d]**	**N**	**% (95% CI)[d]**
PMB648 (B16)	278	81.7 (76.6, 86.0)	273	78.0 (72.6, 82.8)
% hSBA ≥ 1:16				
PMB3010 (A06)	280	95.7 (92.6, 97.8)	275	92.0 (88.1, 94.9)
PMB824 (A12)	277	75.1 (69.6, 80.1)	275	71.3 (65.5, 76.5)
PMB1989 (A19)	275	92.7 (89.0, 95.5)	284	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: The LLOQ is an hSBA titre = 1:16 for A06, A12, and A19; 1:8 for A07, A15, A29, B03, B09, B15, and B16.

a Evaluable immunogenicity population.

b Study 1009 = NCT01830855 and Study 1016 = NCT01352845.

c For third dose, serum was obtained approximately 1 month after vaccination.

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

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) [see section 4.8 Adverse Effects (Undesirable effects)]. The hSBA responses observed after the second or third dose for Groups 1, 2 and 3 are presented in Table 6.

Table 6: Immune Responses Among Subjects 11 to 18 Years of Age Administered Trumenba After Various 2- and 3-Dose Schedules (Study B1971012)[a,b]							
hSBA Strain (fHbp Variant)[c]		**Group 1 (0, 1, and 6 Months)**		**Group 2 (0, 2, and 6 Months)**		**Group 3 (0 and 6 Months)**	
		N	**% or GMT (95% CI)[d]**	**N**	**% or GMT (95% CI)[d]**	**N**	**% or GMT (95% CI)[d]**
PMB80 (A22)	**% hSBA ≥ 1:16**						
	Dose 2	351	73.5 (68.6, 78.0)	344	88.1 (84.2, 91.3)	369	93.2 (90.2, 95.6)
	Dose 3	360	91.4 (88.0, 94.1)	357	95.0 (92.1, 97.0)	--	--
	≥4-Fold rise in hSBA titre (%)						
	Dose 2	343	55.7 (50.3, 61.0)	336	73.8 (68.8, 78.4)	362	80.7 (76.2, 84.6)
	Dose 3	351	78.1 (73.4, 82.3)	349	84.0 (79.7, 87.6)	--	--
	hSBA GMT						
	Before Dose 1	356	11.7 (10.87, 12.58)	352	10.8 (10.10, 11.62)	364	10.8 (10.10, 11.52)
	Dose 2	351	29.0 (26.0 32.5)	344	35.6 (32.2, 39.4)	369	50.6 (45.9, 55. 8)
	Dose 3	360	58.4 (52.4, 64.9)	357	58.3 (53.2, 63.9)	--	--
PMB2001 (A56)	**% hSBA ≥ 1:8**						
	Dose 2	353	96.6 (94.1, 98.2)	339	97.9 (95.8, 99.2)	370	98.4 (96.5, 99.4)

Table 6: Immune Responses Among Subjects 11 to 18 Years of Age Administered Trumenba After Various 2- and 3-Dose Schedules (Study B1971012)[a,b]

hSBA Strain (fHbp Variant)[c]		Group 1 (0, 1, and 6 Months)		Group 2 (0, 2, and 6 Months)		Group 3 (0 and 6 Months)	
		N	% or GMT (95% CI)[d]	N	% or GMT (95% CI)[d]	N	% or GMT (95% CI)[d]
	Dose 3	362	99.4 (98.0, 99.9)	359	98.9 (97.2, 99.7)	--	--
	≥4-Fold rise in hSBA titre (%)						
	Dose 2	338	86.1 (81.9, 89.6)	327	90.5 (86.8, 93.5)	354	90.4 (86.8, 93.3)
	Dose 3	347	93.4 (90.2, 95.8)	347	94.2 (91.2, 96.4)	--	--
	hSBA GMT						
	Before Dose 1	350	6.8 (6.06, 7.64)	348	6.1 (5.54, 6.77)	355	6.7 (6.00, 7.48)
	Dose 2	353	77.3 (68.5, 87.1)	339	94.6 (84.6, 105.7)	370	125.6 (112.6, 140.2)
	Dose 3	362	152.9 (137.2, 170.5)	359	155.6 (140.4, 172.4)	--	--
PMB2948 (B24)	**% hSBA ≥ 1:8**						
	Dose 2	344	62.2 (56.9, 67.4)	337	70.3 (65.1, 75.2)	359	81.1 (76.6, 85.0)
	Dose 3	354	89.0 (85.2, 92.0)	354	88.4 (84.6, 91.6)	--	--
	≥4-Fold rise in hSBA titre (%)						
	Dose 2	341	47.2 (41.8, 52.7)	333	54.1 (48.5, 59.5)	357	65.5 (60.4, 70.5)
	Dose 3	351	74.6 (69.8, 79.1)	350	75.4 (70.6, 79.8)	--	--
	hSBA GMT						
	Before Dose 1	362	5.3 (4.93, 5.75)	356	5.1 (4.77, 5.52)	369	5.0 (4.70, 5.38)
	Dose 2	344	13.8 (12.2, 15.6)	337	14.9 (13.20, 16.73)	359	20.6 (18.3, 23.2)
	Dose 3	354	29.1 (25.9, 32.7)	354	25.6 (23.0, 28.5)	--	--
PMB2707 (B44)	**% hSBA ≥ 1:8**						
	Dose 2	341	54.0 (48.5, 59.3)	331	61.9 (56.5, 67.2)	356	77.5 (72.8, 81.8)
	Dose 3	356	88.5 (84.7, 91.6)	352	86.1 (82.0, 89.5)	--	--
	≥4-Fold rise in hSBA titre (%)						
	Dose 2	339	43.4 (38.0, 48.8)	328	55.2 (49.6, 60.6)	355	66.8 (61.6, 71.6)
	Dose 3	354	82.2 (77.8, 86.0)	349	81.7 (77.2, 85.6)	--	--
	hSBA GMT						
	Before Dose 1	363	4.4 (4.18, 4.54)	357	4.5 (4.24, 4.67)	370	4.5 (4.26, 4.70)
	Dose 2	341	13.1 (11.3, 15.1)	331	15.5 (13.5, 17.9)	356	22.5 (19.6, 25.7)
	Dose 3	356	40.3 (35.2, 46.1)	352	35.0 (30.6, 39.9)	--	--

Table 6: Immune Responses Among Subjects 11 to 18 Years of Age Administered Trumenba After Various 2- and 3-Dose Schedules (Study B1971012)[a,b]

hSBA Strain (fHbp Variant)[c]		Group 1 (0, 1, and 6 Months)		Group 2 (0, 2, and 6 Months)		Group 3 (0 and 6 Months)	
		N	% or GMT (95% CI)[d]	N	% or GMT (95% CI)[d]	N	% or GMT (95% CI)[d]
	Composite response[e]						
	Before Dose 1	339	3.5 (1.8, 6.1)	333	2.4 (1.0, 4.7)	345	3.5 (1.8, 6.0)
	Dose 2	308	45.1 (39.5, 50.9)	311	54.3 (48.6, 60.0)	343	73.5 (68.5, 78.1)
	Dose 3	337	83.1 (78.6, 86.9)	345	81.7 (77.3, 85.7)	--	--

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

Note: The LLOQ is an hSBA titre = 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 titre <1:4 (LOD), a 4-fold response was defined as an hSBA titre ≥1:16. (2) For subjects with a baseline hSBA titre ≥ LOD and < LLOQ, a response is defined as an hSBA titre ≥4 times the LLOQ. (3) For subjects with a baseline hSBA titre ≥ LLOQ, a response is defined as an hSBA titre ≥4 times the baseline titre.

a Evaluable immunogenicity population.

b NCT01299480.

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

d Exact 2-sided confidence interval (Clopper and Pearson) based upon the observed proportion of subjects. For GMTs, CIs are obtained by exponentiating the limits of CIs for the mean logarithm of the hSBA titres (based on the Student t distribution).

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

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 18 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 US, the immunogenicity of concomitantly administered Trumenba and HPV4 vaccine was evaluated in adolescents 11 to 17 years of age. Immune responses were evaluated by comparisons of geometric mean titres (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 US, the immunogenicity of concomitantly administered Trumenba with MenACWYand Tdap vaccines was evaluated in adolescents 10 to 12 years of age. Immune responses were evaluated by comparisons of GMTs for each of 10

MenACWY and Tdap antigens 1 month after the first vaccination. The criterion for the noninferiority margin of 1.5-fold was met for all MenACWYand Tdap antigens.

Persistence of immunity and response to booster vaccination

Study B1971033 was an open-label, follow-up study of subjects previously enrolled in a primary study, including Study B1971012. Subjects attended visits over 4 years for collection of blood samples and received a single booster dose of Trumenba approximately 4 years after receipt of a primary series of 2 or 3 doses of Trumenba.

The hSBA responses 4 years after the primary series and 26 months after the booster dose for subjects enrolled from primary Study B1971012 Group 1 (0, 1, and 6 months), Group 2 (0, 2, and 6 months) and Group 3 (0 and 6 months) are presented in Tables 7 and 8.

Table 7: Persistence of Immune and Booster Responses Among Subjects 11 to 18 Years of Age Administered a Primary Series of Trumenba on a 0-, 1-, and 6-Month; 0-, 2-, and 6-Month; or 0- and 6-Month Schedule and a Booster 4 Years After Primary Series (Study B1971033)[a,b]

hSBA Strain (fHbp Variant)	Time Point	Primary Study B1971012 Vaccine Group (as Randomised)					
		Group 1 (0, 1, and 6 Months)		Group 2 (0, 2, and 6 Months)		Group 3 (0 and 6 Months)	
		N	% (95% CI)[c]	N	% (95% CI)[c]	N	% (95% CI)[c]
PMB80 (A22)	**% hSBA ≥ 1:16**						
	1 Month after last primary dose	59	89.8 (79.2, 96.2)	57	91.2 (80.7, 97.1)	61	98.4 (91.2, 100.0)
	12 Months after last primary dose	99	41.4 (31.6, 51.8)	111	45.0 (35.6, 54.8)	113	36.3 (27.4, 45.9)
	48 Months after last primary dose	59	49.2 (35.9, 62.5)	57	56.1 (42.4, 69.3)	61	55.7 (42.4, 68.5)
	1 Month after booster dose	59	100.0 (93.9, 100.0)	58	100.0 (93.8, 100.0)	60	96.7 (88.5, 99.6)
	12 Months after booster dose	58	74.1 (61.0, 84.7)	54	77.8 (64.4, 88.0)	60	80.0 (67.7, 89.2)
	26 Months after booster dose	0	NE	34	73.5 (55.6, 87.1)	42	61.9 (45.6, 76.4)
PMB2001 (A56)	**% hSBA ≥ 1:8**						
	1 Month after last primary dose	58	100.0 (93.8, 100.0)	57	98.2 (90.6, 100.0)	62	98.4 (91.3, 100.0)
	12 Months after last primary dose	98	73.5 (63.6, 81.9)	109	76.1 (67.0, 83.8)	106	60.4 (50.4, 69.7)
	48 Months after last primary dose	53	43.4 (29.8, 57.7)	55	56.4 (42.3, 69.7)	62	43.5 (31.0, 56.7)
	1 Month after booster dose	57	100.0 (93.7, 100.0)	56	100.0 (93.6, 100.0)	62	98.4 (91.3, 100.0)
	12 Months after booster dose	55	90.9 (80.0, 97.0)	55	89.1 (77.8, 95.9)	59	81.4 (69.1, 90.3)
	26 Months after booster dose	0	NE	29	82.8 (64.2, 94.2)	40	57.5 (40.9, 73.0)
PMB2948 (B24)	**% hSBA ≥ 1:8**						
	1 Month after last primary dose	59	88.1 (77.1, 95.1)	58	91.4 (81.0, 97.1)	60	85.0 (73.4, 92.9)
	12 Months after last primary dose	98	40.8 (31.0, 51.2)	108	49.1 (39.3, 58.9)	103	36.9 (27.6, 47.0)
	48 Months after last primary dose	59	40.7 (28.1, 54.3)	57	49.1 (35.6, 62.7)	62	40.3 (28.1, 53.6)
	1 Month after booster dose	58	100.0 (93.8, 100.0)	57	100.0 (93.7, 100.0)	62	96.8 (88.8, 99.6)

Table 7: Persistence of Immune and Booster Responses Among Subjects 11 to 18 Years of Age Administered a Primary Series of Trumenba on a 0-, 1-, and 6-Month; 0-, 2-, and 6-Month; or 0- and 6-Month Schedule and a Booster 4 Years After Primary Series (Study B1971033)[a,b]

hSBA Strain (fHbp Variant)	Time Point	Primary Study B1971012 Vaccine Group (as Randomised)					
		Group 1 (0, 1, and 6 Months)		Group 2 (0, 2, and 6 Months)		Group 3 (0 and 6 Months)	
		N	% (95% CI)[c]	N	% (95% CI)[c]	N	% (95% CI)[c]
	12 Months after booster dose	58	65.5 (51.9, 77.5)	54	74.1 (60.3, 85.0)	62	77.4 (65.0, 87.1)
	26 Months after booster dose	0	NE	33	78.8 (61.1, 91.0)	42	59.5 (43.3, 74.4)
PMB2707 (B44)	**% hSBA ≥ 1:8**						
	1 Month after last primary dose	58	86.2 (74.6, 93.9)	57	89.5 (78.5, 96.0)	60	81.7 (69.6, 90.5)
	12 Months after last primary dose	100	24.0 (16.0, 33.6)	111	22.5 (15.1, 31.4)	115	16.5 (10.3, 24.6)
	48 Months after last primary dose	57	36.8 (24.4, 50.7)	57	35.1 (22.9, 48.9)	62	12.9 (5.7, 23.9)
	1 Month after booster dose	59	100.0 (93.9, 100.0)	58	100.0 (93.8, 100.0)	61	93.4 (84.1, 98.2)
	12 Months after booster dose	56	75.0 (61.6, 85.6)	53	81.1 (68.0, 90.6)	61	59.0 (45.7, 71.4)
	26 Months after booster dose	0	NE	33	66.7 (48.2, 82.0)	43	62.8 (46.7, 77.0)
Composite response[d]							
	1 Month after last primary dose	57	80.7 (68.1, 90.0)	55	87.3 (75.5, 94.7)	57	77.2 (64.2, 87.3)
	12 Months after last primary dose	55	10.9 (4.1, 22.2)	51	13.7 (5.7, 26.3)	49	20.4 (10.2, 34.3)
	48 Months after last primary dose	51	19.6 (9.8, 33.1)	53	30.2 (18.3, 44.3)	61	9.8 (3.7, 20.2)
	1 Month after booster dose	56	100 (93.6, 100.0)	55	100.0 (93.5, 100.0)	59	91.5 (81.3, 97.2)
	12 Months after booster dose	53	52.8 (38.6, 66.7)	48	64.6 (49.5, 77.8)	57	61.4 (47.6, 74.0)
	26 Months after booster dose	0	NE	27	48.1 (28.7, 68.1)	36	44.4 (27.9, 61.9)

Abbreviations: fHbp=factor H binding protein; hSBA=serum bactericidal assay using human complement; LLOQ = lower limit of quantitation; mITT = modified intent-to-treat; NE=not evaluated (subjects were not followed beyond 12 months post booster).
Note: The LLOQ is an hSBA titre = 1:16 for PMB80 (A22) and 1:8 for PMB2001 (A56), PMB2948 (B24), and PMB2707 (B44).

Note: Serum samples were analysed concurrently in the same serology campaign for all time points except the 12 months post-primary dose time point for which results are from the interim analysis.

a Booster evaluable immunogenicity population. For 12 months after primary dose, specifically for entries for % hSBA≥1:8 or 1:16, the analysis population is Stage 1 mITT immunogenicity population.

b NCT01543087.

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

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

Table 8: Persistence of Immune and Booster Responses (GMT) Among Subjects 11 to 18 Years of Age Administered a Primary Series of Trumenba on a 0-, 1-, and 6-Month; 0-, 2-, and 6-Month; or 0- and 6-Month Schedule and a Booster 4 Years After Primary Series (Study B1971033)[a,b]

hSBA Strain (fHbp Variant) / Time Point		Primary Study B1971012 Vaccine Group (as Randomised)					
		Group 1 (0, 1, and 6 Months)		Group 2 (0, 2, and 6 Months)		Group 3 (0 and 6 Months)	
		N	GMT (95% CI)[c]	N	GMT (95% CI)[c]	N	GMT (95% CI)[c]
PMB80 (A22)	**hSBA GMT**						
	1 Month after last primary dose	59	53.0 (40.4, 69.6)	57	59.5 (45.5, 77.8)	61	55.8 (46.2, 67.4)
	12 Months after last primary dose	99	14.9 (12.6, 17.7)	111	15.8 (13.4, 18.6)	113	15.6 (13.0, 18.8)
	48 Months after last primary dose	59	16.6 (13.0, 21.1)	57	20.7 (15.6, 27.4)	61	16.6 (13.4, 20.5)
	1 Month after booster dose	59	126.5 (102.7, 155.8)	58	176.7 (137.8, 226.7)	60	142.0 (102.9, 196.1)
	12 Months after booster dose	58	33.6 (24.5, 46.1)	54	44.1 (31.2, 62.4)	60	31.6 (23.5, 42.5)
	26 Months after booster dose	0	NE	34	34.7 (23.0, 52.4)	42	27.1 (18.6, 39.6)
PMB2001 (A56)	**hSBA GMT**						
	1 Month after last primary dose	58	158.7 (121.5, 207.3)	57	191.2 (145.8, 250.8)	62	143.1 (109.6, 187.0)
	12 Months after last primary dose	98	25.7 (19.4, 34.0)	109	27.3 (21.0, 35.4)	106	18.5 (13.8, 24.7)
	48 Months after last primary dose	53	10.7 (7.4, 15.3)	55	15.0 (10.2, 22.2)	62	10.8 (7.6, 15.3)
	1 Month after booster dose	57	359.8 (278.7, 464.7)	56	414.8 (298.8, 575.9)	62	313.1 (221.3, 442.8)
	12 Months after booster dose	55	47.3 (34.3, 65.3)	55	64.0 (42.6, 96.2)	59	41.0 (26.7, 62.7)
	26 Months after booster dose	0	NE	29	37.8 (21.3, 67.2)	40	16.0 (9.9, 25.8)
PMB2948 (B24)	**hSBA GMT**						
	1 Month after last primary dose	59	25.6 (19.7, 33.3)	58	30.5 (23.8, 39.1)	60	29.2 (21.5, 39.6)
	12 Months after last primary dose	98	9.7 (7.5, 12.4)	108	11.5 (9.0, 14.6)	103	8.4 (6.7, 10.6)
	48 Months after last primary dose	59	10.7 (7.6, 15.1)	57	11.4 (8.2, 15.9)	62	8.9 (6.8, 11.8)
	1 Month after booster dose	58	94.9 (74.6, 120.9)	57	101.6 (83.1, 124.2)	62	79.1 (60.6, 103.5)
	12 Months after booster dose	58	21.1 (14.2, 31.3)	54	25.7 (17.7, 37.5)	62	22.4 (16.4, 30.5)
	26 Months after booster dose	0	NE	33	24.4 (16.1, 36.8)	42	14.5 (9.9, 21.3)
PMB2707 (B44)	**hSBA GMT**						
	1 Month after last primary dose	58	46.3 (31.7, 67.8)	57	50.2 (35.3, 71.3)	60	35.5 (24.5, 51.4)
	12 Months after last primary dose	100	6.4 (5.2, 7.8)	111	6.0 (5.1, 7.2)	115	5.6 (4.8, 6.5)
	48 Months after last primary dose	57	8.3 (6.3, 11.0)	57	7.6 (5.8, 10.0)	62	4.6 (4.1, 5.1)
	1 Month after booster dose	59	137.3 (100.3, 188.0)	58	135.9 (108.0, 171.0)	61	74.2 (51.6, 106.8)
	12 Months after booster dose	56	23.2 (16.2, 33.2)	53	24.3 (17.8, 33.3)	61	13.3 (9.7, 18.3)

Table 8: Persistence of Immune and Booster Responses (GMT) Among Subjects 11 to 18 Years of Age Administered a Primary Series of Trumenba on a 0-, 1-, and 6-Month; 0-, 2-, and 6-Month; or 0- and 6-Month Schedule and a Booster 4 Years After Primary Series (Study B1971033)[a,b]

hSBA Strain (fHbp Variant)		Primary Study B1971012 Vaccine Group (as Randomised)					
		Group 1 (0, 1, and 6 Months)		Group 2 (0, 2, and 6 Months)		Group 3 (0 and 6 Months)	
	Time Point	N	GMT (95% CI)[c]	N	GMT (95% CI)[c]	N	GMT (95% CI)[c]
	26 Months after booster dose	0	NE	33	16.0 (10.4, 24.7)	43	13.6 (9.8, 18.9)

Abbreviations: fHbp=factor H binding protein; GMT=geometric mean titre; hSBA=serum bactericidal assay using human complement; mITT = modified intent-to-treat; NE=not evaluated (subjects were not followed beyond 12 months post booster).
Note: Serum samples were analysed concurrently in the same serology campaign for all time points except the 12 months post-primary dose time point for which results are from the interim analysis.

a Booster evaluable immunogenicity population. For 12 months after primary dose, the analysis population is Stage 1 mITT immunogenicity population.

b NCT01543087.

c CIs are obtained by exponentiating the limits of CIs for the mean logarithm of the hSBA titres (based on the Student t distribution).

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 minimise 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

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9. DATE OF FIRST APPROVAL

14 September 2017

10. DATE OF REVISION

8 November 2022

® Registered trademark

Summary Table of Changes

Section changed	Summary of new information
Section 4.2	Updated to include information regarding a booster dose
Section 4.8	Updated to include adverse reactions following booster vaccination
Section 5.1	• Two-dose study (B1971057) information added (Tables 2 & 3) • Persistence of immunity and response to booster vaccination (B1971033) information added (Tables 7 & 8) • Tables 4, 5 & 6 updated (data from Studies B1971009, B1971016 and B1971012)