HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use MENHIBRIX safely and effectively. See full prescribing information for MENHIBRIX.

MENHIBRIX (Meningococcal Groups C and Y and Haemophilus b Tetanus Toxoid Conjugate Vaccine)
Solution for Intramuscular Injection
Initial U.S. Approval: 2012

----------INDICATIONS AND USAGE----------

MENHIBRIX is a vaccine indicated for active immunization to prevent invasive disease caused by *Neisseria meningitidis* serogroups C and Y and *Haemophilus influenzae* type b. MENHIBRIX is approved for use in children 6 weeks of age through 18 months of age. (1)

---------- DOSAGE AND ADMINISTRATION ----------

Four doses (0.5 mL each) by intramuscular injection at 2, 4, 6, and 12 through 15 months of age. The first dose may be given as early as 6 weeks of age. The fourth dose may be given as late as 18 months of age. (2.3)

---------- DOSAGE FORMS AND STRENGTHS ----------

Solution for injection supplied as a single-dose vial of lyophilized vaccine to be reconstituted with the accompanying vial of saline diluent. A single dose after reconstitution is 0.5 mL. (3)

----------CONTRAINDICATIONS----------

Severe allergic reaction (e.g., anaphylaxis) after a previous dose of any meningococcal-, *H. influenzae* type b-, or tetanus toxoid-containing vaccine or any component of MENHIBRIX. (4)

---------- WARNINGS AND PRECAUTIONS----------

- If Guillain-Barré syndrome has occurred within 6 weeks of receipt of a prior vaccine containing tetanus toxoid, the decision to give any tetanus toxoid-containing vaccine, including MENHIBRIX, should be based on consideration of the potential benefits and possible risks. (5.1)
- Syncope (fainting) can occur in association with administration of injectable vaccines, including MENHIBRIX. Procedures should be in place to avoid falling injury and to restore cerebral perfusion following syncope. (5.2)
- Apnea following intramuscular vaccination has been observed in some infants born prematurely. Decisions about when to administer an intramuscular vaccine, including MENHIBRIX, to infants born prematurely should be based on consideration of the individual infant's medical status, and the potential benefits and possible risks of vaccination. (5.3)

---------- ADVERSE REACTIONS ----------

Rates of local injection site pain, redness, and swelling ranged from 15% to 46% depending on reaction and specific dose in schedule. Commonly reported systemic events included irritability (62% to 71%), drowsiness (49% to 63%), loss of appetite (30% to 34%), and fever (11% to 26%) (specific rate depended on the event and dose in the schedule). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact GlaxoSmithKline at 1-888-825-5249 or VAERS at 1-800-822-7967 or www.vaers.hhs.gov.

----------DRUG INTERACTIONS----------

Do not mix MENHIBRIX with any other vaccine in the same syringe or vial. (7.1)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 11/2013

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

MENHIBRIX® is indicated for active immunization to prevent invasive disease caused by *Neisseria meningitidis* serogroups C and Y and *Haemophilus influenzae* type b. MENHIBRIX is approved for use in children 6 weeks of age through 18 months of age.

2 DOSAGE AND ADMINISTRATION

2.1 Reconstitution

MENHIBRIX is to be reconstituted only with the accompanying saline diluent. The reconstituted vaccine should be a clear and colorless solution. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. If either of these conditions exists, the vaccine should not be administered.

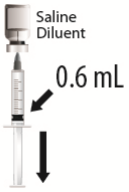

Figure 1. Cleanse both vial stoppers. Withdraw 0.6 mL of saline from diluent vial.

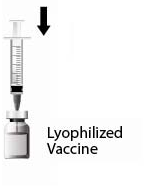

Figure 2. Transfer saline diluent into the lyophilized vaccine vial.

Figure 3. Shake the vial well.

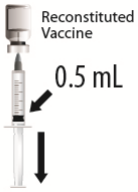

Figure 4. After reconstitution, withdraw 0.5 mL of reconstituted vaccine and administer **intramuscularly**.

2.2 Administration

For intramuscular use only. Do not administer this product intravenously, intradermally, or subcutaneously.

After reconstitution, administer MENHIBRIX immediately.

Use a separate sterile needle and sterile syringe for each individual. The preferred administration site is the anterolateral aspect of the thigh for most infants younger than 1 year of age. In older children, the deltoid muscle is usually large enough for an intramuscular injection.

2.3 Dose and Schedule

A 4-dose series, with each 0.5-mL dose given by intramuscular injection at 2, 4, 6, and 12 through 15 months of age. The first dose may be given as early as 6 weeks of age. The fourth dose may be given as late as 18 months of age.

3 DOSAGE FORMS AND STRENGTHS

MENHIBRIX is a solution for injection supplied as a single-dose vial of lyophilized vaccine to be reconstituted with the accompanying vial of saline diluent. A single dose after reconstitution is 0.5 mL.

4 CONTRAINDICATIONS

Severe allergic reaction (e.g., anaphylaxis) after a previous dose of any meningococcal-, *H. influenzae* type b-, or tetanus toxoid-containing vaccine or any component of this vaccine is a contraindication to administration of MENHIBRIX *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Guillain-Barré Syndrome

If Guillain-Barré syndrome has occurred within 6 weeks of receipt of a prior vaccine containing tetanus toxoid, the decision to give any tetanus toxoid-containing vaccine, including MENHIBRIX, should be based on consideration of the potential benefits and possible risks.

5.2 Syncope

Syncope (fainting) can occur in association with administration of injectable vaccines, including MENHIBRIX. Syncope can be accompanied by transient neurological signs such as visual disturbance, paresthesia, and tonic-clonic limb movements. Procedures should be in place to avoid falling injury and to restore cerebral perfusion following syncope.

5.3 Apnea in Premature Infants

Apnea following intramuscular vaccination has been observed in some infants born prematurely. Decisions about when to administer an intramuscular vaccine, including MENHIBRIX, to infants born prematurely should be based on consideration of the individual infant’s medical status, and the potential benefits and possible risks of vaccination.

5.4 Preventing and Managing Allergic Vaccine Reactions

Prior to administration, the healthcare provider should review the patient's immunization history for possible vaccine hypersensitivity. Epinephrine and other appropriate agents used for the control of immediate allergic reactions must be immediately available should an acute anaphylactic reaction occur.

5.5 Altered Immunocompetence

Safety and effectiveness of MENHIBRIX in immunosuppressed children have not been evaluated. If MENHIBRIX is administered to immunosuppressed children, including children receiving immunosuppressive therapy, the expected immune response may not be obtained.

5.6 Tetanus Immunization

Immunization with MENHIBRIX does not substitute for routine tetanus immunization.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared with rates in the

clinical trials of another vaccine, and may not reflect the rates observed in practice. There is the possibility that broad use of MENHIBRIX could reveal adverse reactions not observed in clinical trials.

A total of 7,521 infants received at least one dose of MENHIBRIX in 6 clinical studies.[1-6] In 5 of these studies, 6,686 children received 4 consecutive doses of MENHIBRIX.[2-6] Across all studies, approximately half of participants were female; 50% were white, 41% were Hispanic, 4% were black, 1% were Asian and 4% were of other racial/ethnic groups.

Two randomized, controlled, pivotal trials enrolled participants to receive 4 doses of MENHIBRIX or a monovalent Haemophilus b Conjugate (Hib) vaccine, administered at 2, 4, 6, and 12 to 15 months of age (Study 009/010[5] and Study 011/012[6]). Together, these trials evaluated safety in 8,571 infants who received at least one dose of MENHIBRIX (N = 6,414) or Hib vaccine (N = 2,157).[5,6]

In Study 009/010[5], conducted in the United States, Australia, and Mexico, 4,180 infants were randomized 3:1 to receive MENHIBRIX or a control US-licensed Hib vaccine. Safety data are available for 3,136 infants who received MENHIBRIX and 1,044 infants who received a control Haemophilus b Conjugate Vaccine (Tetanus Toxoid Conjugate) (PRP-T, manufactured by Sanofi Pasteur SA) at 2, 4, and 6 months of age. For dose 4 administered at 12 to 15 months of age, safety data are available for 2,769 toddlers who received MENHIBRIX and 923 toddlers who received a control Haemophilus b Conjugate Vaccine (Meningococcal Protein Conjugate) (PRP-OMP, manufactured by Merck and Co., Inc.). With doses 1, 2, and 3 of MENHIBRIX or PRP-T, infants concomitantly received PEDIARIX® [Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed, Hepatitis B (Recombinant) and Inactivated Poliovirus Vaccine] and Pneumococcal 7-valent Conjugate Vaccine (Diphtheria CRM_{197} Protein) (PCV7, manufactured by Wyeth Pharmaceuticals, Inc.). With dose 4 of MENHIBRIX or PRP-OMP, toddlers concomitantly received PCV7, Measles, Mumps, and Rubella Virus Vaccine Live (MMR, manufactured by Merck & Co., Inc.), and Varicella Virus Vaccine Live (manufactured by Merck & Co., Inc.).

Data on solicited adverse events were collected by parents/guardians using standardized forms for 4 consecutive days following vaccination with MENHIBRIX or control Hib vaccine (i.e., day of vaccination and the next 3 days).[5] Children were monitored for unsolicited adverse events that occurred in the 31-day period following vaccination and were monitored for serious adverse events, new onset chronic disease, rash, and conditions prompting emergency department visits or physician office visits during the entire study period (6 months following the last vaccine administered). Among participants in both groups, 66% were from the United States, 19% were from Mexico, and 14% were from Australia. Forty-eight percent of participants were female; 64% were white, 22% were Hispanic, 6% were black, 1% were Asian, and 7% were of other racial/ethnic groups.

In the second pivotal study (Study 011/012[6]), conducted in the United States and Mexico and evaluating the same vaccines and vaccination schedule, participants were monitored for serious adverse events, new onset chronic disease, rash, and conditions prompting emergency

department visits during the entire study period (6 months following the last vaccine administered). Among participants in both groups, 30% were from the United States and 70% were from Mexico.

In addition to the pivotal studies, safety data are available from 4 studies which either did not include a fourth dose of MENHIBRIX[1], used a dosing regimen not approved in the United States[2,3], or incorporated a comparator vaccine which was not licensed in the United States.[4] In these studies, participants were monitored for unsolicited adverse events and serious adverse events occurring in the 31–day period following vaccination. In 2 of these studies[3,4], participants were monitored for serious adverse events, new onset chronic disease, rash, and conditions prompting emergency department visits or physician office visits through 6 months after the last vaccination.

Solicited Adverse Events: The reported frequencies of solicited local and systemic adverse events from US participants in Study 009/010 are presented in Table 1.[5] Because of differences in reported rates of solicited adverse events between US and non-US participants, only the solicited adverse event data in US participants are presented. Among the US participants included in Table 1, 48% were female; 76% were white, 10% were black, 4% were Hispanic, 2% were Asian, and 8% were of other racial/ethnic groups.

Table 1. Percentage of US Children from Study 009/010 With Solicited Local and General Adverse Events within 4 Days of Vaccination[a] With MENHIBRIX or Haemophilus b Conjugate Vaccine (Total Vaccinated Cohort)

	MENHIBRIX[b]				Haemophilus b Conjugate Vaccine[b,c]			
	Dose 1	**Dose 2**	**Dose 3**	**Dose 4**	**Dose 1**	**Dose 2**	**Dose 3**	**Dose 4**
Local[d]								
N	2,009	1,874	1,725	1,533	659	612	569	492
Pain, any	46.2	44.6	41.4	42.1	61.6	52.8	49.9	50.4
Pain, grade 3[e]	3.7	3.3	2.3	1.6	11.4	5.1	3.0	5.3
Redness, any	20.6	31.0	35.5	34.6	27.9	33.7	42.2	46.7
Redness, >30 mm	0.1	0.3	0.1	0.7	1.8	0.3	0.4	1.2
Swelling, any	14.7	20.4	23.8	25.4	20.5	20.8	28.6	31.7
Swelling, >30 mm	0.5	0.3	0.3	0.6	1.5	0.2	0.4	0.8
Systemic								
N	2,008-2,009	1,871	1,723	1,535-1,536	659	609-610	569	493-494
Irritability	67.5	70.8	65.8	62.1	76.9	75.1	65.4	66.1
Irritability, grade 3[f]	3.7	4.8	3.3	2.5	7.4	5.6	4.2	4.3
Drowsiness, any	62.8	57.7	49.5	48.7	66.9	61.8	52.4	48.5
Drowsiness, grade 3[g]	2.7	3.2	1.7	2.1	2.7	2.6	1.4	2.0
Loss of appetite, any	33.8	32.1	30.1	32.1	37.6	33.6	30.2	32.5
Loss of appetite, grade 3[h]	0.5	0.7	0.5	1.1	0.3	0.7	1.1	2.2
Fever, ≥100.4°F[i]	18.9	25.9	23.0	11.0	21.4	28.2	23.7	12.6
Fever, ≥102.2°F[i]	1.1	1.9	3.2	1.5	0.9	2.6	2.8	2.0
Fever, >104°F[i]	0.0	0.1	0.3	0.3	0.0	0.0	0.4	0.2

Total Vaccinated Cohort = all participants who received at least one dose of either vaccine.

N = number of participants who completed the symptom sheet for a given symptom at the specified dose.

[a] Within 4 days of vaccination defined as day of vaccination and the next 3 days.

[b] Co-administered with PEDIARIX and PCV7 at doses 1, 2, 3 and PCV7, MMR and varicella vaccines at dose 4.

[c] US-licensed monovalent Haemophilus b Conjugate Vaccine manufactured by Sanofi Pasteur SA for doses 1, 2, and 3 (PRP-T) and by Merck & Co., Inc for dose 4 (PRP-OMP).

[d] Local reactions at the injection site for MENHIBRIX or Haemophilus b Conjugate Vaccine.

[e] Cried when limb was moved/spontaneously painful.

[f] Crying that could not be comforted/prevented normal daily activities.

[g] Prevented normal daily activities.

[h] Not eating at all.

[i] Across both treatment groups, 54%, 56%, and 59% of participants had temperatures measured rectally following doses 1, 2, and 3, respectively; 45%, 44%, and 40% of participants had temperatures measured by the axillary route for doses 1, 2, and 3, respectively. For dose 4, >90% of participants had temperatures measured via the axillary route.

The reported rates of some solicited adverse events in participants from Australia and Mexico varied from those in the United States.[5] For example, in Australia, pain after dose 1 was reported in 28.4% of participants who received MENHIBRIX and 33.3% of control participants, while in Mexico pain after dose 1 was reported in 73.7% of participants who received MENHIBRIX and 79.4% of control participants. Fever after dose 1 was reported in 10.4% of participants who received MENHIBRIX and 10.7% of control participants in Australia, while it was reported in 44.0% of participants who received MENHIBRIX and 35.7% of control participants in Mexico. The reported incidences of pain and fever in US participants after dose 1 are provided in Table 1.

Unsolicited Adverse Events: Among participants who received MENHIBRIX or Hib control vaccine co-administered with US-licensed vaccines at 2, 4, 6 and 12 to 15 months of age[1,3-5], the incidence of unsolicited adverse events reported within the 31-day period following study vaccination (doses 1, 2, and 3) was comparable between MENHIBRIX (61.9%; 2,578/4,166) and PRP-T (62.5%; 1,042/1,666). The incidence of unsolicited adverse events reported within the 31-day period following dose 4 was also comparable between MENHIBRIX (42.5%; 1,541/3,630) and PRP-OMP (41.4%; 520/1,257).

Serious Adverse Events: Following doses 1, 2, and 3[1,3-6], 1.8% (137/7,444) of participants who received MENHIBRIX and 2.1% (59/2,779) of participants who received PRP-T reported at least one serious adverse event within the 31-day period. Up to 6 months following the last vaccine administered (doses 1, 2, and 3) or until administration of dose 4[3-6], 4.8% (365/7,362) of participants who received MENHIBRIX and 5.0% (134/2,697) of participants in the PRP-T group reported at least one serious adverse event.

Following dose 4[3-6], 0.5% (35/6,640) of participants who received MENHIBRIX and 0.5% (12/2,267) of participants who received PRP-OMP reported at least one serious adverse event within the 31-day period. Up to 6 months following the last vaccine administered (dose 4), 2.5% (165/6,640) of participants who received MENHIBRIX and 2.0% (46/2,267) of participants who received PRP-OMP reported at least one serious adverse event.

6.2 Postmarketing Experience

The following adverse events have been spontaneously reported during post-approval use of HIBERIX® (Haemophilus b Conjugate Vaccine [Tetanus Toxoid Conjugate]) in the United States and other countries. These events are relevant because the Haemophilus b capsular polysaccharide tetanus toxoid conjugate is included as a component antigen in both MENHIBRIX and HIBERIX. Because these events are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or to establish a causal relationship to vaccine exposure.

The following adverse events were included based on one or more of the following factors: seriousness, frequency of reporting, or strength of evidence for a causal relationship to HIBERIX.

General Disorders and Administration Site Conditions: Extensive swelling of the vaccinated limb, injection site induration.

Immune System Disorders: Allergic reactions (including anaphylactic and anaphylactoid reactions), angioedema.

Nervous System Disorders: Convulsions (with or without fever), hypotonic-hyporesponsive episode, somnolence, syncope or vasovagal responses to injection.

Respiratory, Thoracic, and Mediastinal Disorders: Apnea.

Skin and Subcutaneous Tissue Disorders: Rash, urticaria.

7 DRUG INTERACTIONS

7.1 Concomitant Vaccine Administration

In clinical studies, MENHIBRIX was administered concomitantly with routinely recommended pediatric US-licensed vaccines *[see Adverse Reactions (6.1) and Clinical Studies (14.2)]*.

If MENHIBRIX is administered concomitantly with other injectable vaccines, they should be given with separate syringes and at different injection sites. MENHIBRIX should not be mixed with any other vaccine in the same syringe or vial.

7.2 Interference With Laboratory Tests

Haemophilus b capsular polysaccharide derived from Haemophilus b Conjugate Vaccines has been detected in the urine of some vaccinees.[7] Urine antigen detection may not have a diagnostic value in suspected disease due to *H. influenzae* type b within 1 to 2 weeks after receipt of a *H. influenzae* type b-containing vaccine, including MENHIBRIX.

7.3 Immunosuppressive Therapies

Immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs, and corticosteroids (used in greater than physiologic doses), may reduce the immune response to MENHIBRIX.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C

Animal reproduction studies have not been conducted with MENHIBRIX. It is also not known whether MENHIBRIX can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity.

8.4 Pediatric Use

Safety and effectiveness of MENHIBRIX in children younger than 6 weeks of age and in children 19 months to 16 years of age have not been established.

11 DESCRIPTION

MENHIBRIX (Meningococcal Groups C and Y and Haemophilus b Tetanus Toxoid Conjugate Vaccine), for intramuscular injection, is supplied as a sterile, lyophilized powder which is reconstituted at the time of use with the accompanying saline diluent. MENHIBRIX contains *Neisseria meningitidis* serogroup C and Y capsular polysaccharide antigens and Haemophilus b capsular polysaccharide (polyribosyl-ribitol-phosphate [PRP]). The *Neisseria meningitidis* C strain and Y strain are grown in semi-synthetic media and undergo heat inactivation and purification. The PRP is a high molecular weight polymer prepared from the *Haemophilus influenzae* type b strain 20,752 grown in a synthetic medium that undergoes heat inactivation and purification. The tetanus toxin, prepared from *Clostridium tetani* grown in a semi-synthetic medium, is detoxified with formaldehyde and purified. Each capsular polysaccharide is individually covalently bound to the inactivated tetanus toxoid. After purification, the conjugate is lyophilized in the presence of sucrose as a stabilizer. The diluent for MENHIBRIX is a sterile saline solution (0.9% sodium chloride) supplied in vials.

When MENHIBRIX is reconstituted with the accompanying vial of saline diluent, each 0.5-mL dose is formulated to contain 5 mcg of purified *Neisseria meningitidis* C capsular polysaccharide conjugated to approximately 5 mcg of tetanus toxoid, 5 mcg of purified *Neisseria meningitidis* Y capsular polysaccharide conjugated to approximately 6.5 mcg of tetanus toxoid, and 2.5 mcg of purified Haemophilus b capsular polysaccharide conjugated to approximately 6.25 mcg of tetanus toxoid. Each dose also contains 96.8 mcg of Tris (trometamol)-HCl, 12.6 mg of sucrose, and ≤0.72 mcg of residual formaldehyde. MENHIBRIX does not contain preservatives. The lyophilized vaccine and saline diluent vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Neisseria meningitidis: The presence of bactericidal anti-capsular meningococcal antibodies has been associated with protection from invasive meningococcal disease.[8] MENHIBRIX induces production of bactericidal antibodies specific to the capsular polysaccharides of serogroups C and Y.

Haemophilus influenzae type b: Specific levels of antibodies to PRP (anti-PRP) have been shown to correlate with protection against invasive disease due to *H. influenzae* type b. Based on data from passive antibody studies[9] and a clinical efficacy study with unconjugated *Haemophilus* b polysaccharide vaccine[10], an anti-PRP concentration of 0.15 mcg/mL has been accepted as a minimal protective level. Data from an efficacy study with unconjugated *Haemophilus* b polysaccharide vaccine indicate that an anti-PRP concentration of ≥1.0 mcg/mL predicts protection through at least a 1-year period.[11,12] These antibody levels have been used to evaluate the effectiveness of *H. influenzae* type b-containing vaccines, including MENHIBRIX.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

MENHIBRIX has not been evaluated for carcinogenic or mutagenic potential, or for impairment of fertility.

14 CLINICAL STUDIES

14.1 Immunological Evaluation

In Study 009/010[5] the immune response to MENHIBRIX and control vaccines was evaluated in a subset of US participants. In this clinical study, MENHIBRIX and Hib control vaccines were administered concomitantly with routinely recommended US-licensed vaccines *[see Adverse Reactions (6.1)]*. Among participants in the ATP immunogenicity cohort for both vaccine groups combined, 47% were female; 81% of participants were white, 8% were black, 4% were Hispanic, 1% were Asian, and 6% were of other racial/ethnic groups.

Study objectives included evaluation of *N. meningitidis* serogroups C (MenC) and Y (MenY) as measured by serum bactericidal assay using human complement (hSBA) and antibodies to PRP as measured by enzyme-linked immunosorbent assay (ELISA) in sera obtained approximately one month (range 21 to 48 days) after dose 3 of MENHIBRIX or PRP-T and approximately 6 weeks (range 35 to 56 days) after dose 4 of MENHIBRIX or PRP-OMP. The hSBA-MenC and hSBA-MenY geometric mean antibody titers (GMTs) and the percentage of participants with hSBA-MenC and hSBA-MenY levels ≥1:8 are presented in Table 2. Anti-PRP geometric mean antibody concentrations (GMCs) and the percentage of participants with anti-PRP levels ≥0.15 mcg/mL and ≥1.0 mcg/mL are presented in Table 3.

Table 2. Bactericidal Antibody Responses Following MENHIBRIX (One Month After Dose 3 and 6 Weeks After Dose 4) in US Children Vaccinated at 2, 4, 6, and 12 to 15 Months of Age (ATP Cohort for Immunogenicity)

	MENHIBRIX Post-Dose 3	**MENHIBRIX Post-Dose 4**
hSBA-MenC	N = 491	N = 331
% ≥1:8	98.8	98.5[a]
95% CI	97.4, 99.6	96.5, 99.5
GMT	968	2040
95% CI	864, 1084	1746, 2383
hSBA-MenY	N = 481	N = 342
% ≥1:8	95.8	98.8[a]
95% CI	93.7, 97.4	97.0, 99.7
GMT	237	1390
95% CI	206, 272	1205, 1602

ATP = according to protocol; CI = confidence interval; GMT = geometric mean antibody titer.

N = number of US children eligible for inclusion in the ATP immunogenicity cohort for whom serological results were available for the post-dose 3 and post-dose 4 immunological evaluations.

[a] Acceptance criteria were met (lower limit of 95% CI for the percentage of participants with hSBA-MenC and hSBA-MenY titers ≥1:8 ≥90% following 4 doses).

Table 3. Comparison of anti-PRP Responses Following MENHIBRIX or Haemophilus b Conjugate Vaccine[a] (One Month After Dose 3 and 6 Weeks After Dose 4) in US Children Vaccinated at 2, 4, 6, and 12 to 15 Months of Age (ATP Cohort for Immunogenicity)

	Post-Dose 3		Post-Dose 4	
	MENHIBRIX	**PRP-T**	**MENHIBRIX**	**PRP-OMP**
Anti-PRP	N = 518	N = 171	N = 361	N = 126
% ≥0.15 mcg/mL	100	98.2	100	100
95% CI	99.3, 100	95.0, 99.6	99.0, 100	97.1, 100
% ≥1.0 mcg/mL	96.3[b]	91.2	99.2[b]	99.2
95% CI	94.3, 97.8	85.9, 95.0	97.6, 99.8	95.7, 100
GMC (mcg/mL)	11.0	6.5	34.9	20.2
95% CI	10.0, 12.1	5.3, 7.9	30.7, 39.6	16.4, 24.9

ATP = according to protocol; anti-PRP = antibody concentrations to *H. influenzae* capsular polysaccharide; CI = confidence interval; GMC = geometric mean antibody concentration.

N = number of US children eligible for inclusion in the ATP immunogenicity cohort for whom serological results were available for the post-dose 3 and post-dose 4 immunological evaluations.

[a] US-licensed monovalent Haemophilus b Conjugate Vaccine for doses 1, 2, and 3 (PRP-T) and for dose 4 (PRP-OMP).

[b] Non-inferiority was demonstrated (lower limit of 95% CI on the group difference of MENHIBRIX minus Haemophilus b Conjugate Vaccine ≥-10%).

14.2 Concomitant Vaccine Administration

In participants who received MENHIBRIX concomitantly with PEDIARIX and PCV7 at 2, 4, and 6 months of age, there was no evidence for reduced antibody response to pertussis antigens (GMC to pertussis toxin, filamentous hemagglutinin, and pertactin), diphtheria toxoid (antibody levels ≥0.1 IU/mL), tetanus toxoid (antibody levels ≥0.1 IU/mL), poliovirus types 1, 2, and 3 (neutralizing antibody levels ≥1:8 to each virus), hepatitis B (anti-hepatitis B surface antigen ≥10 mIU/mL) or PCV7 (antibody levels ≥0.2 mcg/mL and GMC to each serotype) relative to the response in control participants administered PRP-T concomitantly with PEDIARIX and PCV7. The immune responses to PEDIARIX[3,5] and PCV7[3] were evaluated one month following dose 3.

There was no evidence for interference in the immune response to MMR and varicella vaccines (initially seronegative participants with anti-measles ≥200 mIU/mL, anti-mumps ≥51 ED_{50}, anti-rubella ≥10 IU/mL, and anti-varicella ≥1:40) administered at 12 to 15 months of age concomitantly with MENHIBRIX and PCV7 relative to these vaccines administered concomitantly with PRP-OMP and PCV7.[4,5] The immune responses to MMR and varicella vaccines were evaluated 6 weeks post-vaccination. Data are insufficient to evaluate potential interference when a fourth PCV7 dose is administered concomitantly with MENHIBRIX at 12 to 15 months of age.

15 REFERENCES

All NCT numbers are as noted in the National Library of Medicine clinical trial database (see www.clinicaltrials.gov).

1. NCT00127855 (001).
2. NCT00129116 (003/004).
3. NCT00129129 (005/006).
4. NCT00134719 (007/008).
5. NCT00289783 (009/010).
6. NCT00345579/NCT00345683 (011/012).
7. Rothstein EP, Madore DV, Girone JAC, et al. Comparison of antigenuria after immunization with three *Haemophilus influenzae* type b conjugate vaccines. *Pediatr Infect Dis J* 1991;10:311-314.
8. Goldschneider I, Gotschlich EC, Artenstein MS. Human immunity to the meningococcus. I. The role of humoral antibodies. *J Exp Med* 1969;129:1307-1326.
9. Robbins JB, Parke JC, Schneerson R, et al. Quantitative measurement of “natural” and immunization-induced *Haemophilus influenzae* type b capsular polysaccharide antibodies. *Pediatr Res* 1973;7:103-110.
10. Peltola H, Käythy H, Sivonen A, et al. *Haemophilus influenzae* type b capsular polysaccharide vaccine in children: A double-blind field study of 100,000 vaccinees 3 months to 5 years of age in Finland. *Pediatrics* 1977;60:730-737.
11. Käythy H, Peltola H, Karanko V, et al. The protective level of serum antibodies to the capsular polysaccharide of *Haemophilus influenzae* type b. *J Infect Dis* 1983;147:1100.
12. Anderson P. The protective level of serum antibodies to the capsular polysaccharide of *Haemophilus influenzae* type b. *J Infect Dis* 1984;149:1034.

16 HOW SUPPLIED/STORAGE AND HANDLING

MENHIBRIX is available in single-dose vials of lyophilized vaccine, accompanied by vials containing 0.85 mL of saline diluent (packaged without syringes or needles).

Supplied as package of 10 doses (NDC 58160-801-11):

NDC 58160-809-01 Vial of lyophilized vaccine in Package of 10: NDC 58160-809-05

NDC 58160-813-01 Vial of saline diluent in Package of 10: NDC 58160-813-05

16.1 Storage Before Reconstitution

Lyophilized vaccine vials: Store refrigerated between 2° and 8°C (36° and 46°F). Protect vials from light.

Diluent: Store refrigerated or at controlled room temperature between 2° and 25°C (36° and 77°F). Do not freeze. Discard if the diluent has been frozen.

16.2 Storage After Reconstitution

After reconstitution, administer MENHIBRIX immediately. Do not freeze. Discard if the vaccine has been frozen.

17 PATIENT COUNSELING INFORMATION

- Inform parents or guardians of the potential benefits and risks of immunization with MENHIBRIX, and of the importance of completing the immunization series.
- Inform parents or guardians about the potential for adverse reactions that have been temporally associated with administration of MENHIBRIX or other vaccines containing similar components.
- Instruct parents or guardians to report any adverse events to their healthcare provider.
- Give parents or guardians the Vaccine Information Statements, which are required by the National Childhood Vaccine Injury Act of 1986 to be given prior to immunization. These materials are available free of charge at the Centers for Disease Control and Prevention (CDC) website (www.cdc.gov/vaccines).

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