Meningococcal Vaccines

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This Clinical Policy Bulletin addresses meningococcal vaccines.

1. **Medical Necessity**

   Aetna considers meningococcal vaccines, meningococcal conjugate (MenACWY) vaccine (e.g., Menactra, Menveo, and MenQuadfi), serogroup B meningococcal (MenB) vaccine (Bexsero and Trumenba), and meningococcal conjugate (MenABCWY) vaccine (e.g., Penbraya) as a medically necessary preventive service according to the recommendations of the Centers for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices (ACIP).

   Aetna considers CDC ACIP's recommendations for the meningococcal vaccine medically necessary for the following indications:

   1. **Meningococcal Conjugate (MenACWY) Vaccine (e.g., Menactra, Menveo, and MenQuadfi)**

      1. Routine vaccination for all adolescents aged 11 through 18 years of age

         1. ACIP recommends a single dose of MenACWY at age 11 or 12 years followed by a booster dose administered at age 16 years;
         2. Adolescents who receive their first dose at age 13 through 15 years should receive a booster dose at age 16 through 18 years; the booster dose can be administered at any time, as long as a minimum interval of 8 weeks between doses is maintained;
         3. Adolescents who receive a first dose after their 16th birthday do not need a booster dose unless they become at increased risk for meningococcal disease;

      2. Increased Risk for Meningococcal Disease

         1. For members 2 months of age or older with one or more of the following risk factors:

            1. Anatomic asplenia (surgical or congenital) or functional asplenia (including sickle cell disease);
            2. First-year college students who are unvaccinated or under-vaccinated and living in residence halls;
            3. Persistent complement component deficiencies (e.g., C3, C5-C9, properdin, factor H, or factor D) or use of complement inhibitors (e.g., eculizumab [Soliris] or ravulizumab [Ultomiris]);
            4. Human immunodeficiency virus (HIV) infection;
            5. Exposure during an outbreak of meningococcal (*Neisseria meningitidis*) disease;
            6. Persons who are traveling to countries in which *N. meningitidis* is hyperendemic or epidemic*;
            7. Microbiologists who are routinely exposed to *N. meningitidis* isolates*;
            8. Military recruits*;

         2. Boosters for members previously vaccinated and have ongoing risk for meningococcal disease

            1. Anatomic or functional asplenia, persistent complement deficiencies, use a complement inhibitor, HIV infection, and persons who travel to countries in which *N. meningitidis* is

hyperendemic or epidemic and remain at increased risk*:

1. 2 years to 6 years of age - single dose at 3 yrs after primary vaccination and every 5 yrs thereafter;
2. 7 years of age or older - single dose at 5 yrs after primary vaccination and every 5 yrs thereafter;

2. Exposure during an outbreak of *N. meningitidis*:

1. 2 years to 6 years of age - single dose if 3 yrs or more since vaccination;
2. 7 years of age or older - single dose if 5 yrs or more since vaccination;

3. Microbiologists routinely exposed to *N. meningitidis** - single dose at 5 yrs after primary vaccination and every 5 yrs thereafter;
4. Military recruits* - every 5 years based on high-risk travel requirements.

Note: College freshmen living in residence halls do not require a booster unless person becomes at increased risk due to another indication.

3. Members aged 19 through 21 years of age who have not received a dose after their 16th birthday can receive a single MenACWY dose as part of catch-up vaccination.

2. **Serogroup B Meningococcal (MenB) Vaccine (e.g., Bexsero and Trumenba)**

1. For members 10 years of age or older with one or more of the following risk factors for *N. meningitidis* serogroup B meningococcal disease:

1. Anatomic asplenia (surgical or congenital) or functional asplenia (sickle cell disease);
2. Persistent complement component deficiencies (e.g., C3, C5-C9, properdin, factor H, or factor D) or use of complement inhibitors (e.g., eculizumab [Soliris] or ravulizumab [Ultomiris]);
3. Exposure during an outbreak of serogroup B meningococcal (*N. meningitidis*) disease;
4. Microbiologists who are routinely exposed to N. meningitidis isolates*

Note: ACIP does not provide a recommendation for MenB vaccine for the following risk groups: persons with HIV infection, persons who travel to countries where meningococcal (*N. meningitidis*) disease is hyperendemic or epidemic, or military recruits. ACIP does not routinely recommend the MenB vaccine for college students, but it does recommend that college students aged 16 to 23 years consider the vaccine based on shared clinical decision-making. The preferred age for the MenB vaccine is 16 to18 years.

Note: ACIP recommends MenB-4C (Bexsero) or MenB-FHbp (Trumenba) be administered as a 3-dose series at 0, 1–2, and 6 months when given to persons 10 years of age or older at increased risk for serogroup B meningococcal disease. Individuals must receive the same vaccine product for all doses. Bexsero and Trumenba are not interchangeable.

Note: For persons who remain at increased risk for *N. meningitidis* serogroup B meningococcal disease, a single dose booster is considered medically necessary 1 year after primary series completion, then every 2 to 3 years thereafter.

2. Vaccination of healthy adolescents and young adults aged 16 to 23 years with a 2-dose MenB series on the basis of shared clinical decision-making.

Note: Per the CDC, people desiring more rapid protection against serogroup B (e.g., students with less than 6 months before college entry) may receive a 3-dose series (0, 1-2, 6 months) to optimize rapid protection.

Note: booster doses are not recommended by ACIP unless the person becomes at increased risk for meningococcal disease, see Section I.B.1.

3. **Meningococcal Conjugate (MenABCWY) vaccine (e.g., Penbraya)**

Per CDC's ACIP, MenABCWY vaccine may be used when both MenACWY and MenB are indicated at the same visit and members meet *either* of the following:

1. Healthy persons aged 16 through 23 years (routine schedule) when shared clinical decision-making favors administration of MenB vaccine **; or
2. Persons 10 years of age or older who are at increased risk for meningococcal disease (e.g., persistent complement deficiencies, complement inhibitor use, or functional or anatomic asplenia).

Notes: MenABCWY vaccine can be used only when both MenACWY and MenB vaccines are indicated at the same visit. Otherwise, MenACWY and MenB vaccines should be given separately as appropriate (see Sections A and B).

** Per CDC, healthy persons aged 16 through 23 years who receive 1 dose of Penbraya on the basis of shared clinical decision-making should complete the MenB series with a dose of MenB-FHbp (Trumenba) 6 months after the Penbraya vaccine dose was administered.

4. **Meningococcal vaccine for hematopoietic cell transplants (HCT) or solid organ transplant recipients.**

* **Note**: Some plans exclude coverage of immunizations for travel or work. Please check benefit plan descriptions for details.

2. **Experimental, Investigational, or Unproven**

The following procedures/indications are considered experimental, investigational, or unproven because the effectiveness of these approaches has not been established:

1. Meningococcal vaccine for all other indications not listed in Section I
2. Use of saliva testing of antibody levels against meningococcal serogroups for monitoring meningococcal vaccine responses.

3. **Notes**

1. For additional information on the CDC ACIP's recommended vaccination schedule for meningococcal vaccines, see Meningococcal Vaccination: Recommendations of the Advisory Committee on Immunization Practices, United States, 2020.
2. MenHibrix [Meningococcal Groups C and Y and Haemophilus b Tetanus Toxoid Conjugate Vaccine] was discontinued in the U.S in 2016 (GSK, 2016). Meningococcal polysaccharide vaccine (Menomune) was discontinued in the U.S. in February 2017 (CDC, 2017).

CPT Codes / HCPCS Codes / ICD-10 Codes

CPT codes covered if selection criteria are met:

Code	Code Description
***Meningococcal group B vaccine (Trumenba or Bexsero, Penbraya) [for individuals 10 years of age or older]*:**	
90619	Meningococcal conjugate vaccine, serogroups A, C, W, Y, quadrivalent, tetanus toxoid carrier (MenACWY-TT), for intramuscular use
90620	Meningococcal recombinant protein and outer membrane vesicle vaccine, serogroup B, 2 dose schedule, for intramuscular use
90621	Meningococcal recombinant lipoprotein vaccine, serogroup B, 3 dose schedule, for intramuscular use
90623	Meningococcal pentavalent vaccine, conjugated Men A, C, W, Y-tetanus toxoid carrier, and Men B-FHbp, for intramuscular use
90644	Meningococcal conjugate vaccine, serogroups C & Y and Haemophilus influenzae type b vaccine (Hib-MenCY), 4 dose schedule, when administered to children 6 weeks-18 months of age, for intramuscular use
90733	Meningococcal polysaccharide vaccine, serogroups A, C, Y, W-135, quadrivalent (MPSV4), for subcutaneous use
90734	Meningococcal conjugate vaccine, serogroups A, C, Y and W-135, quadrivalent (MenACWY), for intramuscular use

Other CPT codes related to the CPB:

90471	Immunization administration (includes percutaneous, intradermal, subcutaneous, or intramuscular injections); 1 vaccine (single or combination vacctine/toxoid)

Other HCPCS codes related to the CPB:

Code	Code Description
J0596	Injection, c1 esterase inhibitor (recombinant), ruconest, 10 units
J0597	Injection, C-1 esterase inhibitor (human), berinert, 10 units
J0598	Injection, C1 esterase inhibitor (human) cinryze, 10 units
J1300	Injection, eculizumab, 10 mg
Q5139	Injection, eculizumab-aeeb (bkemv), biosimilar, 10 mg

ICD-10 codes covered if selection criteria are met:

B20	Human immunodeficiency virus [HIV] disease
D57.00 - D57.819	Sickle-cell disorders
D84.1	Defects in the complement system
D89.89	Other specified disorders involving the immune mechanism, not elsewhere classified
Q89.01	Asplenia (congenital)
Z02.1	Encounter for pre-employment examination
Z02.3	Encounter for examination for recruitment to armed forces
Z02.89	Encounter for other administrative examinations
Z20.89	Contact with and (suspected) exposure to other communicable diseases
Z20.811	Contact with and (suspected) exposure to meningococcus
Z21	Asymptomatic human immunodeficiency virus [HIV] infection status
Z23	Encounter for immunization
Z59.3	Problems related to living in residential institution
Z65.8	Other specified problems related to psychosocial circumstances [military deployment status]
Z79.810 - Z79.818	Acquired absence of spleen
Z90.81	Acquired absence of spleen
Z94.0	Kidney transplant status
Z94.1	Heart transplant status
Z94.2	Lung transplant status
Z94.3	Heart and lungs transplant status
Z94.4	Liver transplant status
Z94.82	Intestine transplant status
Z94.83	Pancreas transplant status

***Saliva testing of antibody levels*:**

CPT codes not covered for indications listed in the CPB:

***Saliva testing of antibody levels against meningococcal serogroups* - no specific code:**

ICD-10 codes not covered for indications listed in the CPB:

Z01.84	Encounter for antibody response examination [monitoring meningococcal vaccine responses]

Background

Meningococcal meningitis, caused by the bacterium *Neisseria meningitidis*, is a potentially fatal bacterial infection that is characterized by inflammation of the meninges around the brain or spinal cord, which can develop rapidly, often among previously healthy persons. Although the rate of meningococcal disease has declined in the United States since the 1990s, in 2019, there were about 375 total cases of meningococcal disease reported (incidence rate of 0.11 cases per 100,000 persons), with the highest rates being among adolescents and young adults aged 16 through 23 years (CDC, 2022b). Even with appropriate antimicrobial therapy, the overall case-fatality ratio in the United States is 15%, and 10% - 20% of survivors have long-term sequelae such as neurologic disability, limb or digit loss, or hearing loss (Mbaeyi et al, 2020).

Per Mbaeyi and colleagues (2020), *Neisseria meningitidis* is classified into 12 serogroups according to the composition of its polysaccharide capsule. Serogroups A, B, C, W, X, and Y cause most of the disease globally. *N. meningitidis* colonizes mucosal

surfaces of the nasopharynx and is transmitted through direct contact with large-droplet respiratory tract secretions from patients or asymptomatic carriers. Nasopharyngeal carriage rates are highest in adolescents and young adults, who serve as reservoirs for transmission of *N. meningitidis*. Invasive disease is an infrequent consequence of nasopharyngeal colonization.

Three quadrivalent meningococcal conjugate (MenACWY) vaccines are currently licensed and available in the United States:

1. meningococcal groups A, C, W, and Y polysaccharide diphtheria toxoid conjugate vaccine (MenACWY-D) (Menactra);
2. meningococcal groups A, C, W, and Y oligosaccharide diphtheria CRM197 conjugate vaccine (MenACWY-CRM) (Menveo); *and*
3. meningococcal groups A, C, W, and Y polysaccharide tetanus toxoid conjugate vaccine (MenACWY-TT) (MenQuadfi).

Two serogroup B meningococcal (MenB) vaccines are licensed and available in the United States:

1. MenB-FHbp (Trumenba); *and*
2. MenB-4C (Bexsero).

One pentavalent meningococcal conjugate (MenABCWY) vaccine, MenACWY-TT/MenB-FHbp (Penbraya), is currently licensed and available in the United States.

MenB-FHbp consists of two purified recombinant lipidated FHbp antigens, one from each FHbp subfamily (A and B). MenB-4C consists of three recombinant proteins (neisserial adhesin A [NadA], factor H binding protein [FHbp] fusion protein from subfamily B, and neisserial heparin binding antigen [NhbA] fusion protein) and outer membrane vesicles (OMVs) containing outer membrane protein porin A (PorA) serosubtype P1.4. Two additional licensed meningococcal vaccines are no longer available in the United States:

1. a quadrivalent (serogroups A, C, W, and Y) meningococcal polysaccharide vaccine (MPSV4) (Menomune – A/C/Y/W-135); *and*
2. a combined Haemophilus influenzae type b and meningococcal serogroups C and Y conjugate vaccine (Hib-MenCY-TT) (MenHibrix) (Mbaeyi et al, 2020).

In October 2016, GlaxoSmithKline (GSK) issued a letter to the customer regarding the decision to discontinue the manufacture and sale of MenHibrix® [Meningococcal Groups C and Y and Haemophilus b Tetanus Toxoid Conjugate Vaccine] in the US. This decision was made due to low demand for the vaccine and the resulting opportunity to shift GSK vaccine production capacity to other GSK vaccines with greater customer demand. MenHibrix continued to be available to order through February 2017 or until inventory levels were depleted (whichever occurred first), at which point, GSK discontinued availability of the vaccine (GSK, 2016).

In February 2017, Sanofi Pasteur, the manufacturer of meningococcal polysaccharide vaccine (Menomune), announced that it is discontinuing production of the vaccine. The company expects to be able to ship orders to providers until mid-2017. The remaining lots will expire in June or in September 2017, according to Sanofi Pasteur (CDC, 2017).

Efforts are under way to reduce the global incidence of meningococcal disease and other causes of meningitis through a strategy that includes optimizing the use of current vaccines as well as developing additional vaccines, such as an expanded conjugate vaccine that includes serogroups A, C, W, Y, and X for use in sub-Saharan Africa (Mbaeyi et al, 2020).

In October 2023, a pentavalent meningococcal vaccine (MenACWY-TT/MenB-FHbp [Penbraya, Pfizer Inc.]) was licensed for use in persons 10 through 25 years of age. MenACWY-TT/MenB-FHbp contains the same components as those in two existing meningococcal vaccines: *N. meningitidis* polysaccharide groups A, C, W, and Y conjugated to tetanus toxoid carrier protein (MenACWY-TT), and two recombinant lipidated factor H–binding protein (FHbp) variants from *N. meningitidis* serogroup B (MenB-FHbp [Trumenba, Pfizer Inc.]) (Collins et al, 2024).

Advisory Committee on Immunization Practices (ACIP) Recommendations

The Centers for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices (ACIP) released updated meningococcal vaccination recommendations which now include routine use of serogroup B meningococcal (MenB) vaccine series among individuals aged 10 years or older who have increased risk for serogroup B meningococcal disease, including persons with complement deficiency, use a complement inhibitor, have asplenia, or are microbiologists routinely exposed to isolates of *N. meningitidis*. In addition, ACIP recommends administration of booster doses of the MenB vaccine for persons at increased risk for serogroup B meningococcal disease (Mbaeyi et al, 2020).

Groups identified for increased risk for meningococcal disease include the following (Mbaeyi et al, 2020):

- Persons with persistent complement component deficiencies
- Use of complement inhibitors (e.g., the currently licensed eculizumab [Soliris] and its long-acting derivative ravulizumab [Ultomiris] monoclonal antibody therapies that block C5) is associated with a substantially increased risk for meningococcal disease

- Persons with anatomic or functional asplenia (including sickle cell disease) appear to be at increased risk for meningococcal disease and, compared with healthy persons, have a higher mortality rate (40%–70%) from the disease
- Persons living with HIV infection
- Microbiologists routinely exposed to *N. meningitidis* isolates
- Persons at increased risk during an outbreak of meningococcal disease, which account for approximately 5% of cases in the U.S.
- Travelers to countries where meningococcal disease is hyperendemic or epidemic, such as the meningitis belt of sub-Saharan Africa
- College freshman living in residence halls. Although not assessed outside of outbreak settings, participation in a fraternity or sorority is an additional risk factor during serogroup B meningococcal disease outbreaks
- Military recruits
- Several outbreaks of serogroup C meningococcal disease have been reported among men who have sex with men (MSM) in the United States. MSM have also been shown to be at increased risk for meningococcal disease outside of out.

In general, ACIP recommends routine vaccination with a quadrivalent meningococcal conjugate vaccine (MenACWY) for all persons aged 11 to 18 years. ACIP also provides recommendations for the MenB vaccine for persons aged 16 to 23 years on the basis of shared clinical decision-making to provide short-term protection against most strains of serogroup B meningococcal disease. The preferred age for MenB vaccination is 16 to 18 years (Mbaeyi et al, 2020).

MenACWY Vaccine ACIP Recommendations

- ACIP recommends a single dose of MenACWY at age 11 or 12 years followed by a booster dose administered at age 16 years.
- Routine vaccination of persons aged 2 months and older at increased risk for meningococcal disease (dosing schedule varies by age and indication, and interval for booster dose varies by age at time of previous vaccination):
    - Persons with certain medical conditions including anatomic or functional asplenia, complement component deficiencies (e.g., C3, C5-C9, properdin, factor H, or factor D), complement inhibitor (e.g., eculizumab [Soliris] or ravulizumab [Ultomiris]) use, or human immunodeficiency virus infection
    - Microbiologists with routine exposure to *Neisseria meningitidis* isolates
    - Persons at increased risk during an outbreak (e.g., in community or organizational settings, and among men who have sex with men [MSM])
    - Persons who travel to or live in countries in which meningococcal disease is hyperendemic or epidemic
    - Unvaccinated or undervaccinated first-year college students living in residence halls
    - Military recruits.

- Booster doses for previously vaccinated persons who become or remain at increased risk.
- Children who received MenACWY at age 10 years do not need an additional dose at age 11 to 12 years but should receive the booster dose at age 16 years.
- Children who received MenACWY before age 10 years and with no ongoing risk for meningococcal disease for which boosters are recommended should still receive MenACWY according to the recommended adolescent schedule, with the first dose at age 11 to12 years and a booster dose at age 16 years.
- Children who received MenACWY before age 10 years and for whom boosters are recommended because of an ongoing increased risk for meningococcal disease (e.g., those with complement deficiency, HIV infection, or asplenia) should follow the booster schedule for persons at increased risk.
- Adolescents who receive their first dose at age 13 to 15 years should receive a booster dose at age 16 to18 years; the booster dose can be administered at any time, as long as a minimum interval of 8 weeks between doses is maintained.
- Adolescents who receive a first dose after their 16th birthday do not need a booster dose unless they become at increased risk for meningococcal disease.
- First-year college students living in residence halls should receive at least 1 dose of MenACWY within 5 years before college entry. The preferred timing of the most recent dose is on or after their 16th birthday. If only 1 dose of vaccine was administered before the 16th birthday, a booster dose should be administered before enrollment. Adolescents who received a first dose after their 16th birthday do not need another dose before college entry unless greater than 5 years have elapsed since the dose.
- Persons aged 19 to 21 years who have not received a dose after their 16th birthday can receive a single MenACWY dose as part of catch-up vaccination.

Note: MenACWY primary vaccinations are licensed as a single dose in persons aged 2 to 55 years for MenACWY-D and MenACWY-CRM or 2 years and older for MenACWY-TT. Two-dose primary series is considered off-label.

ACIP provides the following recommendations for MenACWY booster vaccination:

- Aged 11 to 21 years: 1 dose at age 16 yrs if first dose administered before 16th birthday. Although routine vaccination is only recommended for adolescents aged 11 to 18 yrs, MenACWY may be administered to persons aged 19 to 21 yrs who have not received a dose after their 16th birthday

- For persons 2 years of age and older who remain at increased risk of persistent complement deficiencies (including patients using a complement inhibitor), anatomic and functional asplenia (including sickle cell disease), or HIV infection:
    - Aged 2 to 6 yrs: Single dose at 3 yrs after primary vaccination and every 5 yrs thereafter
    - Aged 7 yrs of age or older: Single dose at 5 yrs after primary vaccination and every 5 yrs thereafter
- For microbiologists who remain at risk for exposure to isolates of *N. meningitidis*:

  Single dose at 5 yrs after primary vaccination and every 5 yrs thereafter
- If person previously vaccinated and identified as being at increased risk during an outbreak:
    - Aged 2 to 6 yrs: Single dose if greater than or equal to 3 yrs since vaccination
    - Aged 7 years or older: Single dose if greater than or equal to 5 yrs since vaccination
- For persons who travel to countries where meningococcal disease is hyperendemic or epidemic and person remains at increased risk:
    - Aged 2 to 7 yrs: Single dose at 3 yrs after primary vaccination and every 5 yrs thereafter
    - Aged 7 yrs or older: Single dose at 5 yrs after primary vaccination and every 5 yrs thereafter
- College freshmen living in residence halls: boosters are not routinely recommended unless person becomes at increased risk due to another indication
- Military recruits: Every 5 yrs on basis of assignment. Vaccination recommendations for military personnel are made by the U.S. Department of Defense on the basis of high-risk travel requirements.

Note: MenACWY vaccines are licensed in the United States only for a single booster dose for persons aged 15 to 55 years for MenACWY-D and MenACWY-CRM or aged 15 years or older for MenACWY-TT. Booster doses administered outside of these ages or administration of greater than 1 booster dose are considered off-label (Mbaeyi et al, 2020).

MenACWY vaccines are interchangeable; however, the same vaccine product is recommended but not required for all doses. MenACWY vaccines can be administered simultaneously with other vaccines indicated for this age group, but at a different anatomic site, if feasible. MenACWY-TT, which is conjugated to tetanus toxoid, is only licensed for the prevention of meningococcal disease. Thus, use of this vaccine does not replace doses or affect the dosing intervals of routinely recommended tetanus toxoid–containing vaccines in any age group (Mbaeyi et al, 2020).

MenB Vaccine ACIP Recommendations

ACIP recommends routine vaccination of persons aged 10 years or older at increased risk for meningococcal disease (dosing schedule varies by vaccine brand; boosters should be administered at 1 year after primary series completion, then every 2 - 3 years thereafter). Note that MenB vaccines are licensed in the United States only for persons aged 10 to 25 years. Vaccination of persons aged 26 years and older is considered off-label. Furthermore, administration of booster doses is considered off-label.

MenB vaccine may be considered for persons with the following risks for meningococcal disease:

- Persons with certain medical conditions, such as anatomic or functional asplenia, complement component deficiencies, or complement inhibitor use
- Microbiologists with routine exposure to *N. meningitidis* isolates
- Persons at increased risk during an outbreak (e.g., in community or organizational settings, and among MSM)

MenB vaccination is not routinely recommended for all adolescents. Instead, ACIP recommends a 2-dose MenB series for persons aged 16 to 23 years on the basis of shared clinical decision-making, which refers to an individually based vaccine recommendation informed by a decision-making process between the health care provider and the patient or parent/guardian. The preferred age for MenB vaccination is 16 to 18 years. Booster doses are not recommended unless the person becomes at increased risk for meningococcal disease (Mbaeyi et al, 2020).

For adolescents who are not otherwise at increased risk for meningococcal disease (e.g., due to complement deficiency or asplenia), a 2-dose series of MenB vaccine should be administered as follows: 2 doses of MenB-FHbp administered at 0 and 6 months or 2 doses of MenB-4C administered at 0 and greater than or equal to 1 month. If the second dose of MenB-FHbp is administered earlier than 6 months after the first dose, a third dose should be administered at least 4 months after the second dose. Either of the MenB vaccines can be used when indicated. ACIP does not state a product preference. However, MenB vaccines are not interchangeable, and the same vaccine product must be used for all doses. If one MenB dose was received but the vaccine product is unknown, the series must be restarted with either product to ensure completion of a 2-dose series using the same product. If 2 doses were administered using different MenB products, one product should be selected for

administration of an additional dose at an appropriate interval to ensure valid completion of a MenB series; the dose from the product not selected for series completion should be considered invalid. For situations in which a MenB dose or doses must be repeated, a minimum interval of 4 weeks should be used between any 2 doses. MenB vaccines can be administered simultaneously with other vaccines indicated for this age group, but at a different anatomic site, if feasible (Mbaeyi et al, 2020).

The ACIP recommends booster doses for previously vaccinated persons who become or remain at increased risk. For persons 10 years of age or older with persistent complement deficiencies (including patients using a complement inhibitor), anatomic and functional asplenia (including sickle cell disease), or are microbiologists routinely exposed to isolates of *N. meningitidis*, ACIP recommends single booster dose at 1 yr after completion of primary vaccination and every 2–3 yrs thereafter. If person was previously vaccinated and identified as being at increased risk during an outbreak, ACIP recommends a single booster dose if greater than or equal to 1 yr after MenB primary series completion (≥6 mos interval might also be considered by public health professionals) (Mbaeyi et al, 2020).

In October 2024, the ACIP updated their guidance on the dosing of MenB vaccinations. In August, the FDA approved a new dosing schedule for MenB-4C vaccine (Bexsero; GlaxoSmithKline) to include a 3-dose series, previously limited to a 2-dose series. Labeling for MenB-FHbP vaccine (Trumenba) includes both a 2-dose series and a 3-dose series. Thus, the ACIP met to review whether a 3-dose series for Bexsero could align with the recommendations for Trumenba. The ACIP provided the following recommendations:

- MenB-4C (Bexsero) may be administered as a 2-dose series at 0 and 6 months when given to healthy adolescents and young adults aged 16–23 years based on shared clinical decision-making for the prevention of serogroup B meningococcal disease;
- MenB-4C (Bexsero) may be administered as a 3-dose series at 0, 1–2, and 6 months when given to persons aged ≥10 years at increased risk for serogroup B meningococcal disease (i.e., persons with anatomic or functional asplenia, complement component deficiencies, or complement inhibitor use; microbiologists routinely exposed to *N. meningitidis* isolates; and persons at increased risk during an outbreak);
- People desiring more rapid protection against serogroup B (e.g., students with less than 6 months before college entry) may receive a 3-dose series (0, 1–2, 6 months) to optimize rapid protection.

As a reminder, MenB vaccines are licensed in the United States only for persons aged 10 to 25 years. Vaccination of persons aged 26 years and older is considered off-label.

Pregnancy and Lactation ACIP Recommendations

Pregnant and lactating women should receive MenACWY vaccine if indicated. Because limited data are available for MenB vaccination during pregnancy, vaccination with MenB should be deferred unless the woman is at increased risk and, after consultation with her health care provider, the benefits of vaccination are considered to outweigh the potential risks.

Altered Immunocompetence

Persons with functional or anatomic asplenia (including sickle cell disease) and persistent complement component deficiency (including persons taking eculizumab [Soliris]) are at increased risk for meningococcal disease and should receive both MenACWY and MenB vaccines.

A hematopoietic cell transplant (HCT) results in immunosuppression because of the hematopoietic ablative therapy administered before the transplant, drugs used to prevent or treat graft-versus-host disease, and, in some cases, from the underlying disease process necessitating transplantation. HCT recipients of all ages are at increased risk for certain vaccine-preventable diseases, including diseases caused by encapsulated bacteria (i.e., pneumococcal, meningococcal, and Hib infections). As a result, HCT recipients who received vaccines prior to their HCT should be revaccinated routinely after HCT, regardless of the source of the transplanted stem cells. Vaccination or revaccination doses of pneumococcal vaccines, DTaP vaccine, Hib vaccine, hepatitis A vaccine, hepatitis B vaccine, meningococcal vaccines, IPV, inactivated influenza vaccines, and human papillomavirus (HPV) vaccines (for individuals aged 9-26 years) are recommended after HCT (CDC, 2022c).

Certain immunosuppressive medications are administered to prevent solid organ transplant rejection (CDC, 2022c).

MenABCWY Vaccine ACIP Recommendations

In April 2024, the ACIP recommended that MenACWY-TT/MenB-FHbp (Penbraya, Pfizer Inc.) may be used when both MenACWY and MenB are indicated at the same visit for:

- Healthy persons aged 16–23 years (routine schedule) when shared clinical decision-making favors administration of MenB vaccine and
- Persons aged ≥10 years who are at increased risk for meningococcal disease (e.g., because of persistent complement deficiencies, complement inhibitor use, or functional or anatomic asplenia).

The licensed dosing interval for MenACWY-TT/MenB-FHbp is 6 months. Data are not available regarding safety or immunogenicity of MenACWY-TT/MenB-FHbp with dosing intervals exceeding 12 months. Healthy adolescents and young adults aged 16–23 years who receive 1 dose of MenACWY-TT/MenB-FHbp (Penbraya) on the basis of shared clinical decision-making should complete the MenB series with a dose of MenB-FHbp 6 months after the pentavalent vaccine dose was administered (Collins et al, 2024).

Persons at increased risk for meningococcal disease who receive a dose of MenACWY-TT/MenB-FHbp and are recommended to receive additional doses of MenACWY and MenB <6 months after a dose of pentavalent meningococcal vaccine should receive separate MenACWY and MenB-FHbp vaccines rather than MenACWY-TT/MenB-FHbp. MenACWY-TT/MenB-FHbp may be used for booster doses in persons who remain at increased risk if a booster dose of both MenACWY and MenB are indicated at the same visit. MenACWY-TT/MenB-FHbp doses deviating from the licensed 6-month interval can be considered valid for MenACWY or MenB if the timing would otherwise have been valid for that component (Collins et al, 2024).

Meningococcal Conjugate (MenACWY) Vaccines

U.S. Food and Drug Administration (FDA)-Approved Indications

- Menactra (Sanofi Pasteur Inc) is a meningococcal (Groups A, C, Y and W-135) polysaccharide diphtheria toxoid conjugate vaccine indicated for active immunization to prevent invasive meningococcal disease caused by *Neisseria meningitidis* serogroups A, C, Y and W-135. Menactra is approved for use in individuals 9 months through 55 years of age. Menactra does not prevent *N. meningitidis* serogroup B disease.
- Menveo (GlaxoSmithKline) is a meningococcal (Groups A, C, Y, and W-135) oligosaccharide diptheria CRm197 conjugate vaccine indicated for active immunization to prevent invasive meningococcal disease caused by *Neisseria meningitidis* serogroups A, C, Y, and W-135. Menveo is approved for use in persons aged 2 months through 55 years. Menveo does not prevent *N. meningitidis* serogroup B infections.
- MenQuadfi (Sanofi Pasteur Inc) is a meningococcal (Groups A, C, Y, W) conjugate vaccine indicated for active immunization for the prevention of invasive meningococcal disease caused by *Neisseria meningitidis* serogroups A, C, W, and Y. MenQuadfi is approved for use in individuals 2 years of age and older. MenQuadfi does not prevent *N. meningitidis* serogroup B disease.

Menactra is supplied as a 0.5 mL dose for intramuscular injection. The primary vaccination schedule, per the label, include children 9 through 23 months of age: two doses, three months apart; and a single dose for individuals 2 through 55 years of age.

Booster vaccination is labeled as a single dose for individuals 15 through 55 years of age at continued risk for meningococcal disease, if at least 4 years have elapsed since the prior dose.

Persons previously diagnosed with Guillain-Barré syndrome (GBS) may be at increased risk of GBS following receipt of Menactra. The decision to give Menactra should take into account the potential benefits and risks. Common (≥10%) solicited adverse events in infants and toddlers 9 and 12 months of age were injection site tenderness, erythema, and swelling; irritability, abnormal crying, drowsiness, appetite loss, vomiting, and fever. Common (≥10%) solicited adverse events in individuals 2 through 55 years of age who received a single dose were injection site pain, redness, induration, and swelling; anorexia and diarrhea. Other common solicited adverse events were irritability and drowsiness (2-10 years of age), headache, fatigue, malaise, and arthralgia (11-55 years of age). Safety and effectiveness of Menactra have not been established in children younger than 9 months of age, pregnant women, nursing mothers, and adults older than 55 years of age (Sanofi Pasteur, 2018).

Menveo is available as a solution for intramuscular injection supplied as a lyophilized MenA conjugate vaccine component to be reconstituted with the accompanying MenCYW-135 liquid conjugate vaccine component. A single dose after reconstitution is 0.5 mL. The primary vaccination schedule, pre the label, include the following:

- In children initiating vaccination at 2 months of age, Menveo is to be administered as a 4-dose series at 2, 4, 6, and 12 months of age.
- In children initiating vaccination at 7 months through 23 months of age, Menveo is to be administered as a 2-dose series with the second dose administered in the second year of life and at least 3 months after the first dose.
- In individuals aged 2 through 55 years Menveo is to be administered as a single dose.

Booster vaccination is labeled as a single dose to be administered to individuals aged 15 through 55 years who are at continued risk for meningococcal disease if at least 4 years have elapsed since a prior dose of a meningococcal (serogroups A, C, Y, W-135) conjugate vaccine.

Menveo carries the following warnings and precautions:

- Appropriate medical treatment must be available should an acute allergic reaction, including an anaphylactic reaction, occur following administration of Menveo.
- Syncope, sometimes resulting in falling injury, has been reported following vaccination with Menveo. Vaccines should be observed for at least 15 minutes after vaccine administration.

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

Common solicited adverse reactions (≥10%) among children initiating vaccination at 2 months of age and receiving the 4-dose series were tenderness (24% to 41%) and erythema at injection site (11% to 15%), irritability (42% to 57%), sleepiness (29% to 50%), persistent crying (21% to 41%), change in eating habits (17% to 23%), vomiting (5% to11%), and diarrhea (8% to 16%). Common solicited adverse reactions (≥10%) among children initiating vaccination at 7 months through 23 months of age and receiving the 2-dose series were tenderness (10% to 16%) and erythema at injection site (12% to 15%), irritability (27% to 40%), sleepiness (17% to 29%), persistent crying (12-21%), change in eating habits (12% to 20%), and diarrhea (10% to 16%). Common solicited adverse reactions (≥10%) among children aged 2 through 10 years who received MENVEO were injection site pain (31%), erythema (23%), irritability (18%), induration (16%), sleepiness (14%), malaise (12%), and headache (11%). Common solicited adverse reactions (≥10%) among adolescents and adults who received a single dose of Menveo were pain at the injection site (41%), headache (30%), myalgia (18%), malaise (16%), and nausea (10%). Similar rates of solicited adverse reactions were observed following a single booster dose (GSK, 2020).

MenQuadfi is available as a solution for injection in 0.5 mL single-dose vials for intramuscular injection. The primary vaccination, per the label, include administration of a single dose for individuals 2 years of age and older. Per the label, a booster vaccination is administered as a single dose to individuals 15 years of age and older who are at continued risk for meningococcal disease if at least 4 years have elapsed since a prior dose of meningococcal (groups A, C, W, Y) conjugate vaccine.

The most commonly reported adverse reactions (≥10%) following a primary dose were as follows:

- Children 2 through 9 years of age, pain (38.6%), erythema (22.6%), and swelling (13.8%) at the injection site; malaise (21.1%), myalgia (20.1%), and headache (12.5%).
- Adolescents aged 10 through 17 years of age, injection site pain (34.8%–45.2%), myalgia (27.4%–35.3%), headache (26.5%–30.2%), and malaise (19.4%–26.0%).
- Adults aged 18 through 55 years, injection site pain (41.9%), myalgia (35.6%), headache (29.0%), and malaise (22.9%).
- Adults 56 years of age and older, pain at the injection site (25.5%), myalgia (21.9%), headache (19.0%), and malaise (14.5%).

In adolescents and adults, rates of solicited adverse reactions following a booster dose were comparable to those observed following primary vaccination (Sanofi Pasteur, 2021).

Serogroup B Meningococcal (MenB) Vaccines

U.S. Food and Drug Administration (FDA)-Approved Indications

- Bexsero (GlaxoSmithKline) is indicated for active immunization to prevent invasive disease caused by *Neisseria meningitidis* serogroup B. Bexsero is approved for use in individuals aged 10 through 25 years. Approval of Bexsero is based on demonstration of immune response, as measured by serum bactericidal activity against three serogroup B strains representative of prevalent strains in the United States. The effectiveness of Bexsero against diverse serogroup B strains has not been confirmed.
- Trumenba (Pfizer Inc) is indicated for active immunization to prevent invasive disease caused by *Neisseria meningitidis* serogroup B. Trumenba is approved for use in individuals 10 through 25 years of age. The effectiveness of the two-dose schedule of Trumenba against diverse *N. meningitidis* serogroup B strains has not been confirmed.

The FDA granted accelerated approval of Bexsero (meningococcal group B Vaccine [recombinant, adsorbed]) for active immunization to prevent invasive meningococcal disease caused by serogroup B in adolescents and young adults from 10 years through 25 years of age (Novartis, 2015). As part of the accelerated approval process, the manufacturer will complete its ongoing studies to confirm the effectiveness of Bexsero against diverse serogroup B strains.

In phase II and phase III studies, Bexsero demonstrated a protective immune response in adolescents and young adults after two doses. Approval of Bexsero is based on demonstration of immune response, as measured by serum bactericidal activity against three serogroup B strains representative of prevalent strains in the United States. The effectiveness of Bexsero against diverse serogroup B strains has not been confirmed (Novartis, 2015).

Three studies evaluating Bexsero’s effectiveness were conducted in Canada, Australia, Chile, and the United Kingdom in approximately 2,600 adolescents and young adults (FDA, 2015). Among study participants who received two doses of Bexsero, after vaccination, 62 to 88 percent had antibodies in their blood that killed three different *N. meningitidis* serogroup B strains in tests carried out in a laboratory, compared with 0 to 23 percent before vaccination. These three strains are representative of strains that cause serogroup B meningococcal disease in the U.S.

The tolerability profile of Bexsero was also demonstrated as part of a CDC-sponsored clinical trial conducted in approximately 15,000 individuals at Princeton University and the University of California, Santa Barbara (UCSB) during meningitis B outbreaks

on these college campuses (Novartis, 2015). The safety data from the CDC clinical trial are consistent with results observed in previous studies.

Bexsero is supplied as a suspension for intramuscular injection in 0.5 mL single-dose prefilled syringes, which is labed to be administered as 2 doses (0.5 mL each) at least 1 month apart. The label for Bexsero cautions that the tip caps of the prefilled syringes contain natural rubber latex which may cause allergic reactions. The most common solicited adverse reactions observed in clinical trials were pain at the injection site (≥83%), myalgia (≥48%), erythema (≥45%), fatigue (≥35%), headache (≥33%), induration (≥28%), nausea (≥18%), and arthralgia (≥13%).

In August 2024, the FDA approved Bexsero 3-dose series (at 0, 1-2, and 6 months) for active immunization to prevent invasive disease caused by *Neisseria meningitidis* serogroup B for use in individuals aged 10 through 25 years. Previously approved as a 2-dose series.

Trumenba was approved by the FDA via the accelerated approval regulatory pathway was announced October 2014 by the U.S. Food and Drug Administration (FDA). Trumemba is licensed in the United States to prevent invasive meningococcal disease caused by Neisseria meningotidis serogroup B in individuals 10 to 25 years of age (FDA, 2014).

The FDA announced that three randomized studies that were conducted in the United states and Europe in approximately 2,800 adolescents showed that after vaccination, 82 percent had antibodies against four different serogroup B strains compared with less than 1 percent before vaccination (FDA, 2014). The effectiveness of Trumenba against diverse serogroup B strains has not been confirmed (Pfizer, 2015).

The safety of Trumenba was assessed in approximately 4,500 patients who received the vaccine in studies conducted in the United States, Europe, and Australia, in which the most commonly reported side effects were pain and swelling at the injection site, headache, diarrhea, muscle pain, joint pain, fatigue and chills (FDA, 2014). Individuals with weakened immune systems may have a reduced immune response (Pfizer, 2015).

Trumenba is also supplied as a suspension for intramuscular injection in 0.5 mL single-dose prefilled syringe. However, Trumenba is labeled to be administered as a two-dose or three-dose schedule. For two-dose schedule, Trumenba dose (0.5 mL) is labeled to be administered at 0 and 6 months. Per the label, if the second dose is administered earlier than 6 months after the first dose, a third dose should be administered at least 4 months after the second dose. The three-dose schedule, per the labeled recommendation, includes administration of 0.5 mL at 0, 1-2, and 6 months. Syncope (fainting) can occur in association with administration of injectable vaccines, including Trumenba. Procedures should be in place to avoid injury from fainting. The most common solicited adverse reactions in adolescents and young adults were pain at the injection site (≥85%), fatigue (≥60%), headache (≥55%), and muscle pain (≥35%).

Beeslaar and colleagues (2018) stated that invasive meningococcal disease (IMD) caused by *Neisseria meningitidis* is a potentially devastating condition that can result in death and is associated with serious long-term sequelae in survivors. Vaccination is the preferred preventative strategy. Quadri-valent polysaccharide-based vaccines that protect against infection caused by meningococcal serogroups A, C, W, and Y are not effective against meningococcal serogroup B (MenB), which was responsible for approximately 60 % and 35 % of confirmed IMD cases in the European Union (EU) and the U.S. in 2016, respectively. A recombinant protein MenB vaccine (MenB-FHbp [bivalent rLP2086; Trumenba®]) has been approved for protection against MenB infection in persons 10 to 25 years of age in the U.S. and Canada and for individuals greater than or equal to 10 years of age in the EU and Australia. In these regions, MenB-FHbp is approved as a 2- or 3-dose primary vaccination schedule. These investigators reviewed the current evidence supporting administration of MenB-FHbp as a 2-dose primary vaccination schedule. They also reviewed different contexts in which a 2- or 3-dose primary vaccination schedule might be preferred (e.g., routine prospective vaccination versus outbreak control).

Meningococcal Conjugate (MenABCWY) Vaccine

U.S. Food and Drug Administration (FDA)-Approved Indications

- Penbraya (Pfizer Inc) is indicated for active immunization to prevent invasive disease caused by Neisseria meningitidis serogroups A, B, C, W, and Y. Penbraya is approved for use in individuals 10 through 25 years of age.

In 2023, the FDA approved Penbraya (meningococcal groups A, B, C, W and Y vaccine) as the first and only pentavalent vaccine that provides coverage against the most common serogroups causing meningococcal disease in adolescents and young adults 10 through 25 years of age. Penbraya combines the components from two meningococcal vaccines, Trumenba® (meningococcal group B vaccine) and Nimenrix® (meningococcal groups A, C, W-135, and Y conjugate vaccine) to help protect against the five most common meningococcal serogroups that cause the majority of invasive meningococcal disease. FDA approval was based on data from Phase 2 and Phase 3 trials, which demonstrated that Penbraya has robust immunogenicity non-inferior to Trumenba® plus Menveo® for all serogroups and was well-tolerated with a favorable safety profile.

Penbraya is supplied in a kit that includes a vial of lyophilized MenACWY component (a sterile white powder), a prefilled syringe containing the MenB component and a vial adapter. After reconstitution, a single dose of 0.5 mL is administered intramuscularly

as part of a 2-dose series 6 months apart.

The most commonly reported (15% or more) solicited adverse reactions after Dose 1 and Dose 2, respectively, were pain at the injection site (89% and 84%), fatigue (52% and 48%), headache (47% and 40%), muscle pain (26% and 23%), injection site redness (26% and 23%), injection site swelling (25% and 24%), joint pain (20% and 18%), and chills (20% and 16%).

Use of Saliva Testing of Antibody Levels Against Meningococcal Serogroups for Monitoring Meningococcal Vaccine Responses

van Ravenhorst and associates (2018) noted that meningococcal infection starts with colonization of the upper respiratory tract. Mucosal immunity is important for protection against acquisition and subsequent meningococcal carriage. In this study, these researchers evaluated salivary antibody levels against meningococcal serogroup A (MenA), W (MenW) and Y (MenY) after vaccination with a quadri-valent MenACWY conjugated vaccine. They also compared salivary meningococcal serogroup C (MenC) antibody levels after monovalent MenC and quadri-valent MenACWY conjugated vaccination. Healthy participants, who had received MenC conjugate vaccine between 14 months and 3 years of age, received a (booster) MenC or MenACWY vaccination at age 10 to 15 years. MenA-, MenC-, MenW- and MenY-polysaccharide (PS) specific IgG and IgA levels in saliva and serum and PS specific secretory component levels in saliva were measured using the fluorescent-bead-based multiplex immunoassay. MenACYW vaccination increased salivary PS-specific IgA (2-fold) and IgG levels(greater than 10-fold) for MenA, MenY, and MenW. After 1 year, salivary IgA levels had returned to baseline levels. Both vaccines induced an increase in salivary MenC-PS specific IgA (greater than 3-fold) and IgG (greater than 100-fold), with higher levels after MenC as compared to MenACWY vaccination. The antibody decay rate of MenC in saliva between 1 month and 1 year was similar for both vaccines. The overall correlation between serum and saliva IgA levels was low (R = 0.39, R = 0.58, R = 0.31, and R = 0.36 for MenA, MenC, MenW and MenY, respectively). Serogroup-PS specific IgG levels between serum and saliva correlated better (R ranged from 0.51 to 0.88). The authors concluded that both primary and booster parenteral meningococcal conjugate vaccination induced antibody levels in saliva for all targeted sero-groups. These investigators stated that salivary samples might be an interesting screening tool to measure vaccine responses after both primary and booster vaccination, especially in geographical areas where blood collection is challenging. They noted that while a minimal threshold needs yet to be assessed, IgG antibodies in saliva samples could potentially serve as surrogate of protection.

van Ravenhorst and colleagues (2019) stated that mucosal antibodies against capsular polysaccharides offer protection against acquisition and carriage of encapsulated bacteria like *Neisseria meningitidis* serogroup C. Measurements of salivary antibodies as replacement for blood testing has important (cost-effective) advantages, especially in studies that evaluate the impact of large-scale vaccination or in populations in which blood sampling is difficult. These researchers estimated a threshold for meningococcal IgG salivary antibody levels to discriminate between unprotected and protected vaccinated individuals. MenA-, MenC-, MenW- and MenY- PS specific IgG levels in serum and saliva from participants in a meningococcal vaccination study were measured using the fluorescent-bead-based multiplex immunoassay. Functional antibody titers in serum against the 4 serogroups were measured with serum bactericidal assay using rabbit complement (rSBA). A threshold for salivary IgG was determined by analysis of receiver operating characteristic (ROC) curves using a serum rSBA titer of greater than or equal to 128 as correlate of protection. The area under the curve (AUC) was calculated to quantify the accuracy of the salivary test and was considered adequate when greater than or equal to 0.80. The optimal cut-off was considered adequate when salivary IgG cut-off levels provided specificity of greater than or equal to 90 %. True positive rate (sensitivity), positive predictive value (PPV), and negative predictive value (NPV) were calculated to explore the possible use of salivary antibody levels as a surrogate of protection. The best ROC curve (AUC of 0.95) was obtained for MenC, with an estimated minimum threshold of MenC-PS specific salivary IgG greater than or equal to 3.54 ng/ml as surrogate of protection. An adequate AUC (greater than 0.80) was also observed for MenW and MenY with an estimated minimal threshold of 2.00 and 1.82 ng/ml, respectively. When applying these thresholds, all (100 %) samples collected 1 month and 1 year after the (booster) meningococcal vaccination, that were defined as protective in the saliva test for MenC, MenW and MenY, corresponded with concomitant serum rSBA titer greater than or equal to 128 for the respective meningococcal serogroups. The authors concluded that the saliva test offered an alternative screening tool to monitor protective vaccine responses up to 1 year after meningococcal vaccination against MenC, MenW and MenY. These researchers stated that future, large, longitudinal vaccination studies evaluating also clinical protection against IMD or carriage acquisition are needed to validate the currently proposed threshold in saliva.

The authors stated that a drawback of this study was that only samples of children aged 10 to 15 years were used here to identify the salivary thresholds. Thus, these salivary thresholds as surrogate of protection have to be validated in other large meningococcal vaccine trials, preferably studies that include participants with a wide age range. furthermore, samples were collected only up to 1 year after vaccination. Whether saliva samples could be used as a surrogate of protection in the long-term after vaccination has to be examined as well.

References

The above policy is based on the following references:

1. Abitbol V, Sohn W-Y, Horn M, Safadi MAP. Safety and immunogenicity of co-administered meningococcal serogroup B (4CMenB) vaccine: A literature review. Hum Vaccin Immunother. 2023;19(2):2245705.
2. Advisory Committee on Immunization Practices (ACIP) Centers for Disease Control and Prevention (CDC). Report from the Advisory Committee on Immunization Practices (ACIP): Decision not to recommend routine vaccination of all children aged 2-10 years with quadrivalent meningococcal conjugate vaccine (MCV4). MMWR Morb Mortal Wkly Rep. 2008;57(17):462-465.
3. Alderfer J, Srivastava A, Isturiz R, et al. Concomitant administration of meningococcal vaccines with other vaccines in adolescents and adults: A review of available evidence. Hum Vaccin Immunother. 2019;15(9):2205-2216.
4. American Academy of Pediatrics (AAP). Meningococcal infections. In: 2003 Red Book: Report of the Committee on Infectious Diseases. G. Peter, ed. 25th ed. Elk Grove Village, IL: AAP; 2003.
5. American Academy of Pediatrics Committee on Infectious Diseases. Prevention and control of meningococcal disease: Recommendations for use of meningococcal vaccines in pediatric patients. Pediatrics. 2005;116(2):496-505.
6. American Academy of Pediatrics, Committee on Infectious Diseases. Meningococcal disease prevention and control strategies for practice-based physicians (Addendum: recommendations for college students). Pediatrics. 2000;106(6):1500-1504.
7. American Academy of Pediatrics, Committee on Infectious Diseases; Canadian Paediatric Society, Infectious Diseases and Immunization Committee. Meningococcal disease prevention and control strategies for practice-based physicians. Pediatrics. 1996;97(3):404-412.
8. Aventis Pasteur Inc. Menactra meningococcal (Groups A, C, Y and W-135) polysaccharide diphtheria toxoid conjugate vaccine. Product Labeling. 4714-5. Swiftwater, PA: Aventis Pasteur; January 2005.
9. Aventis Pasteur Inc. Menomune-A/C/Y/W-135 meningococcal polysaccharide vaccine groups A, C, Y and W-135 combined. Prescribing Information. 4813/4875. Swiftwater, PA: Aventis-Pasteur; January 2003.
10. Avery RK, Michaels M. Update on immunizations in solid organ transplant recipients: What clinicians need to know. Am J Transplant. 2008;8(1):9-14.
11. Basta NE, Mahmoud AA, Wolfson J, et al. Immunogenicity of a meningococcal B vaccine during a university outbreak. N Engl J Med. 2016;375(3):220-228.
12. Beeslaar J, Absalon J, Balmer P, et al. Clinical data supporting a 2-dose schedule of MenB-FHbp, a bivalent meningococcal serogroup B vaccine, in adolescents and young adults. Vaccine. 2018;36(28):4004-4013.
13. Castilla J, Cenoz MG, Abad R, et al. Effectiveness of a meningococcal group B vaccine (4CMenB) in children. N Engl J Med. 2023;388(5):427-438.
14. Centers for Disease Control and Prevention (CDC), Advisory Committee on Immunization Practices (ACIP), Vaccines for Children Program. Meningococcus. Vaccines to prevent meningococcal disease. Resolution No. 2/05-2. Atlanta, GA: CDC; February 10, 2005.
15. Centers for Disease Control and Prevention (CDC), Advisory Committee on Immunization Practices. Revised recommendations of the Advisory Committee on Immunization Practices to vaccinate all persons aged 11-18 years with meningococcal conjugate vaccine. MMWR Morb Mortal Wkly Rep. 2007;56(31):794-795.
16. Centers for Disease Control and Prevention (CDC), Advisory Committee on Immunization Practices. Notice to readers: Recommendation from the Advisory Committee on Immunization Practices (ACIP) for use of quadrivalent meningococcal conjugate vaccine (MCV4) in children aged 2--10 years at increased risk for invasive meningococcal disease. MMWR Morb Mortal Wkly Rep. 2007:56(48):1265-1266.
17. Centers for Disease Control and Prevention (CDC), Advisory Committee on Immunization Practices (ACIP). Updated recommendation from the Advisory Committee on Immunization Practices (ACIP) for use of 7-valent pneumococcal conjugate vaccine (PCV7) in children aged 24-59 months who are not completely vaccinated. MMWR Morb Mortal Wkly Rep. 2008;57(13):343-344.
18. Centers for Disease Control and Prevention (CDC), National Immunization Program (NIP). ACIP recommends meningococcal vaccine for adolescents and college freshman. Meningococcal conjugate vaccine. Meningococcal (groups A, C, Y and W-135) conjugate vaccine (MCV-4). In the Spotlight for the Public. NIP Public Home. Atlanta, GA: CDC; February 10, 2005.
19. Centers for Disease Control and Prevention (CDC). Control and prevention of serogroup C meningococcal disease: Evaluation and management of suspected outbreaks: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep. 1997;46(RR-5):1-21.
20. Centers for Disease Control and Prevention (CDC). Infant meningococcal vaccination: Advisory Committee on Immunization Practices (ACIP) recommendations and rationale. MMWR Morb Mortal Wkly Rep. 2013;62(3):52-54.
21. Centers for Disease Control and Prevention (CDC). Licensure of a meningococcal conjugate vaccine (Menveo) and guidance for use - Advisory Committee on Immunization Practices (ACIP), 2010. MMWR. 2010;59(09);273.
22. Centers for Disease Control and Prevention (CDC). Meningococcal disease and college students. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep. 2000;49(RR-7):13-20.
23. Centers for Disease Control and Prevention (CDC). Meningoccal disease: Causes and how it spreads. Atlanta, GA: CDC; February 2022a. Available at: https://www.cdc.gov/meningococcal/about/causes-transmission.html. Accessed March 17, 2022.
24. Centers for Disease Control and Prevention (CDC). Meningococcal disease: Clinical information. Atlanta, GA: CDC; February 2022b. Available at: https://www.cdc.gov/meningococcal/clinical-info.html #:~:text=In%202019%2C%20there%20were%20about, a%20second%20peak%20in%20adolescence. Accessed March 17, 2022.

25. Centers for Disease Control and Prevention (CDC). Risk-based indications for meningococcal vaccination. Meningococcal Disease [website]. Atlanta, GA: CDC; June 26, 2024. Available at: https://www.cdc.gov/. Accessed October 30, 2024.
26. Centers for Disease Control and Prevention (CDC). Prevention and control of meningococcal disease: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep. 2000;49(RR-7):1-10.
27. Centers for Disease Control and Prevention (CDC). Recommended adult immunization schedule --- United States, 2002--2003. MMWR Morbid Mortal Wkly Rep. 2002;51(40):904-908.
28. Centers for Disease Control and Prevention (CDC). Travelers' health: Clinical update. Atlanta, GA: CDC; February 2017. Available at: https://wwwnc.cdc.gov/travel/news-announcements/menomune-discontinuation#:~:text=Clinical%20Update-,Menomune%20(meningococcal%20polysaccharide%20vaccine)%20discontinuation,to%20providers%20until%20mid%2D2017. Accessed March 14, 2022.
29. Centers for Disease Control and Prevention (CDC). Vaccine information statement (interim): Serogroup B meningococcal vaccine. Atlanta, GA: CDC; 2015.
30. Centers for Disease Control and Prevention (CDC). Vaccine recommendations and guidelines of the ACIP: Altered immunocompetence. Atlanta, GA: CDC; February 2022c. Available at: https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/immunocompetence.html. Accessed March 17, 2022.
31. Centers for Disease Control and Prevention (CDC), Division of News and Electronic Media. CDC Advisory Committee on Immunization Practices Recommends HibMenCY for Infants at Increased Risk for Meningococcal Disease. Atlanta, GA: CDC; October 24, 2012.
32. Committee in Infectious Diseases, American Academy of Pediatrics. Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention; American Academy of Family Physicians. Recommended childhood immunization schedule -- United States, 2002. Pediatrics. 2002;109(1):162.
33. Collins JP, Crowe SJ, Ortega-Sanchez IR, et al. Use of the Pfizer pentavalent meningococcal vaccine among persons aged ≥10 years: Recommendations of the Advisory Committee on Immunization Practices - United States, 2023. MMWR Morb Mortal Wkly Rep. 2024;73(15):345-350.
34. Committee on Infectious Diseases. Policy statement: Updated recommendations on the use of meningococcal vaccines. Pediatrics. 2014;134(2):400-403.
35. Conterno LO, Silva Filho CR, Ruggeberg JU, Heath PT. Conjugate vaccines for preventing meningococcal C meningitis and septicaemia. Cochrane Database Syst Rev. 2006;(3):CD001834.
36. Fiorito TM, Baird GL, Alexander-Scott N, et al. Adverse events following vaccination with bivalent rLP2086 (Trumenba®): An observational, longitudinal study during a college outbreak and a systematic review. Pediatr Infect Dis J. 2018;37(1):e13-e19.
37. Folaranmi T, Rubin L, Martin SW, et al. Use of serogroup B meningococcal vaccines in persons aged ≥10 years at increased risk for serogroup B meningococcal disease: Recommendations of the Advisory Committee on Immunization Practices, 2015. MMWR Morb Mortal Wkly Rep. 2015;64(22):608-612.
38. Gardner P. Clinical practice. Prevention of meningococcal disease. N Engl J Med. 2006;355(14):1466-1473.
39. Gasparini R, Tregnaghi M, Keshavan P, et al. Safety and immunogenicity of a quadrivalent meningococcal conjugate vaccine and commonly administered vaccines after coadministration. Pediatr Infect Dis J. 2016;35(1):81-93.
40. GlaxoSmithKline (GSK). Bexsero (meningoccal group B vaccine) suspension, for intramuscular injection. Prescribing Information. Research Triangle Park, NC: GSK; revised August 2024.
41. GlaxoSmithKline (GSK). Letter to the customer from GlaxoSmithKline regarding the decision to discontinue the manufacture and sale of MenHibrix [meningococcal groups C and Y and haemophilus b tetanus toxoid conjugate vaccine] in the U.S. Research Triangle Park, NC: GSK; October 2016.
42. GlaxoSmithKline (GSK). Menveo [meningococcal (groups A, C, Y, and W-135) oligosaccharide diphtheria CRM197 conjugate vaccine]. Prescribing Information. Research Triangle Park, NC: GSK; revised July 2020.
43. Gossger N, Snape MD, Yu LM, et al; European MenB Vaccine Study Group. Immunogenicity and tolerability of recombinant serogroup B meningococcal vaccine administered with or without routine infant vaccinations according to different immunization schedules: A randomized controlled trial. JAMA. 2012;307(6):573-582.
44. Hale SF, Camaione L, Lomaestro BM. MenHibrix: A new combination meningococcal vaccine for infants and toddlers. Ann Pharmacother. 2014;48(3):404-411.
45. Hitt E. ACIP recommends meningococcal booster dose. Medscape Medical News. New York, NY: Medscape; October 28, 2010. Available at: http://www.medscape.com/viewarticle/731392?src=smo_id. Accessed October 29, 2010.
46. Howdieshell TR, Heffernan D, Dipiro JT; Therapeutic Agents Committee of the Surgical Infection Society. Surgical infection society guidelines for vaccination after traumatic injury. Surg Infect (Larchmt). 2006;7(3):275-303.
47. Kelleher JA, Raebel MA. Meningococcal vaccine use in college students. Ann Pharmacother. 2002;36(11):1776-1784.
48. Kim DK, Bridges CB, Harriman KH; Advisory Committee on Immunization Practices (ACIP). Advisory Committee on Immunization Practices recommended immunization schedule for adults aged 19 years or older: United States, 2016. Ann Intern Med. 2016;164(3):184-194.
49. Kim DK, Riley LE, Harriman KH, et al. Advisory Committee on Immunization Practices Recommended Immunization Schedule for Adults Aged 19 Years or Older - United States, 2017. MMWR Morb Mortal Wkly Rep. 2017;66(5):136-138.
50. Li G, Cappuccini F, Marchevsky NG, et al; COV006 study team. Safety and immunogenicity of the ChAdOx1 nCoV-19 (AZD1222) vaccine in children aged 6-17 years: A preliminary report of COV006, a phase 2 single-blind, randomised, controlled trial. Lancet. 2022;399(10342):2212-2225.
51. Makris MC, Polyzos KA, Mavros MN, et al. Safety of hepatitis B, pneumococcal polysaccharide and meningococcal polysaccharide vaccines in pregnancy: A systematic review. Drug Saf. 2012;35(1):1-14.

52. Marshall GS, Abbing-Karahagopian V, Marshall HS, et al. A comprehensive review of clinical and real-world safety data for the four-component serogroup B meningococcal vaccine (4CMenB). Expert Rev Vaccines. 2023;22(1):530-544.
53. McMillan M, Chandrakumar A, Wang HLR, et al. Effectiveness of meningococcal vaccines at reducing invasive meningococcal disease and pharyngeal Neisseria meningitidis carriage: A systematic review and meta-analysis. Clin Infect Dis. 2021;73(3):e609-e619.
54. Mbaeyi SA, Bozio CH, Duffy J, et al. Meningococcal vaccination: Recommendations of the Advisory Committee on Immunization Practices, United States, 2020. MMWR Recomm Rep. 2020;69(9):1-41.
55. National Meningitis Association (NMA). New meningococcal immunization recommendations seek to protect adolescents and college students from potentially fatal meningococcal disease. Press Release. Lexington Park, MD: NMA; February 10, 2005.
56. National Organization for Rare Disorders (NORD). Meningococcal meningitis. NORD Rare Disease Database. Danbury, CT; NORD; 2015.
57. Novartis AG. Novartis Bexsero vaccine approved by FDA for the prevention of meningitis B, the leading cause of bacterial meningitis in the US. Media Release. Basel, Switzerland: Novartis; January 23, 2015.
58. Novartis Vaccines and Diagnostics, Inc. Bexsero (meningococcal group B vaccine) suspension for intramuscular injection. Prescribing Information. Cambridge, MA: Novartis; January 2015.
59. Nwogu IB, Jones M, Langley T. Economic evaluation of meningococcal serogroup B (MenB) vaccines: A systematic review. Vaccine. 2021;39(16):2201-2213.
60. Pace D, Khatami A, McKenna J, et al. Immunogenicity of reduced dose priming schedules of serogroup C meningococcal conjugate vaccine followed by booster at 12 months in infants: Open label randomised controlled trial. BMJ. 2015;350:h1554.
61. Patel M, Lee CK. Polysaccharide vaccines for preventing serogroup A meningococcal meningitis. Cochrane Database Syst. Rev. 2005:(1):CD001093.
62. Patton ME, Stephens D, Moore K, MacNeil JR. Updated recommendations for use of MenB-FHbp serogroup B meningococcal vaccine - Advisory Committee on Immunization Practices, 2016. MMWR Morb Mortal Wkly Rep. 2017;66(19):509-513.
63. Pellegrino P, Perrone V, Radice S, et al. Immunogenicity of meningococcal quadrivalent (serogroup A, C, W135 and Y) tetanus toxoid conjugate vaccine: Systematic review and meta-analysis. Pharmacol Res. 2015;92:31-39.
64. Pereira P, Benninghoff B, Moerman L, et al. Systematic literature review on the safety and immunogenicity of rotavirus vaccines when co-administered with meningococcal vaccines. Hum Vaccin Immunother. 2020;16(11):2861-2872.
65. Peterson ME, Li Y, Bita A, et al; Meningococcal Surveillance Group (in alphabetical order). Meningococcal serogroups and surveillance: A systematic review and survey. J Glob Health. 2019;9(1):010409.
66. Pfizer Inc. CDC Advisory Committee on Immunization Practices votes to recommend serogroup B meningococcal disease vaccination for persons at increased risk. Press Release. New York, NY: Pfizer; February 26, 2015.
67. Pfizer Inc. Penbraya - meningococcal gropups a,b,c, w, and y vaccine. Prescribing Information. New York, NY: Pfizer; revised September 2024.
68. Pfizer Inc. Trumenba (meningococcal group B vaccine) suspension for intramuscular use. Prescribing Information. Philadelphia, PA: Pfizer; revised June 2024.
69. Pichichero M, Casey J, Blatter M, et al. Comparative trial of the safety and immunogenicity of quadrivalent (A,C,Y,W-135) meningococcal polysaccharide-diphtheria conjugate vaccine versus quadrivalent polysaccharide vaccine in two- to ten-year-old children. Pediatr Infect Dis J. 2005;24:57-62.
70. Reisinger KS, Block SL, Collins-Ogle M, et al; Protocol 025 Investigators. Safety, tolerability, and immunogenicity of Gardasil given concomitantly with Menactra and Adacel. Pediatrics. 2010;125(6):1142-1151.
71. Rubin l, Cohn A, MacNeil J, Messonnier N. Infant meningococcal vaccination: Advisory Committee on Immunization Practices (ACIP) recommendations and rationale. Morbidity and Mortality Weekly Report. 2013;62(3): 52-54.
72. Sanofi Pasteur, Inc. Menactra (meningococcal (groups A, C, Y and W-135) polysaccharide diphtheria toxoid conjugate vaccine) for intramuscular injection. Prescribing Information. Swiftwater, PA: Sanofi Pasteur; revised April 2018.
73. Sanofi Pasteur, Inc. Menomune - A/C/Y/W-135, meningococcal polysaccharide vaccine, groups A, C, Y and W-135 combined, solution for subcutaneous injection. Prescribing Information. Swiftwater, PA: Sanofi Pasteur; revised March 2016.
74. Sanofi Pasteur, Inc. MenQuadfi (meningococcal (groups A,C, Y and W) conjugate vaccine. Prescribing Information. Swiftwater, PA: Sanofi Pasteur; revised October 2021.
75. Schillie SF. Introduction to MenB-4C (Bexsero) interval and dosing label change. National Center for Immunization & Respiratory Diseases. Presentation to Advisory Committee on Immunization Practices, Atlanta, GA, October 24, 2024. Available at: https://www.cdc.gov/acip/downloads/slides-2024-10-23-24/04-mening-Schillie-508.pdf. Accessed October 30, 2024.
76. Schilling A, Parra MM, Gutierrez M, et al. Coadministration of a 9-valent human papillomavirus vaccine with meningococcal and Tdap vaccines. Pediatrics. 2015;136(3):e563-e572.
77. Splete H. ACIP votes to extend Menactra to high-risk infants. Elsevier Global Medical News. Morristown, NJ: Elsevier; June 23, 2011. Available at: http://infoviewer.biz/infodisplay/story/imn062220111630165996.html?APP=7&CU=imn5804. Accessed July 13, 2011.
78. Swift D. ACIP updates recommendations for adult vaccines. Medscape Medical News. February 3, 2020. Available at: https://www.medscape.com/viewarticle/924692.
79. Tapia MD, Sow SO, Naficy A, et al. Meningococcal serogroup ACWYX conjugate vaccine in Malian toddlers. N Engl J Med. 2021;384(22):2115-2123.

80. U.S. Food and Drug Administration (FDA) First vaccine approved by FDA to prevent serogroup B Meningococcal disease. FDA News Release. Silver Spring, MD: FDA; October 29, 2014.
81. U.S. Food and Drug Administration (FDA). FDA approves a second vaccine to prevent serogroup B meningococcal disease. FDA News Release. Silver Spring, MD: FDA; January 23, 2015.
82. van Ravenhorst MB, den Hartog G, van der Klis FRM, et al. Induction of salivary antibody levels in Dutch adolescents after immunization with monovalent meningococcal serogroup C or quadrivalent meningococcal serogroup A, C, W and Y conjugate vaccine. PLoS One. 2018;13(4):e0191261.
83. van Ravenhorst MB, van der Klis FRM, van Rooijen DM, et al. Use of saliva to monitor meningococcal vaccine responses: Proposing a threshold in saliva as surrogate of protection. BMC Med Res Methodol. 2019;19(1):1.
84. Wall RA. Meningococcal disease: Treatment and prevention. Ann Med. 2002;34(7-8):624-634.
85. Wildes SS, Tunkel AR. Meningococcal vaccines: A progress report. BioDrugs. 2002;16(5):321-329.
86. World Health Organization. WHO position paper, Meningococcal A conjugate vaccine: Updated guidance, February 2015. Vaccine. 2018;36(24):3421-3422.

Policy History

- Last Review 02/05/2025

  Effective: 11/23/1999

  Next Review: 04/10/2025

- Review History
- Definitions

Additional Information

- Clinical Policy Bulletin Notes