State of California—Health and Human Services Agency
California Department of Public Health

MARK B HORTON, MD, MSPH
Director

ARNOLD SCHWARZENEGGER
Governor

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TO: California Vaccines for Children (VFC) Program Providers

FROM: John Talarico, D.O., M.P.H, Chief
Center for Infectious Diseases
Division of Communicable Disease Control, Immunization Branch

SUBJECT: MENVEO®, MENINGOCOCCAL [SEROGROUPS A, C, Y AND W-135, CRM_{193} PROTEIN] CONJUGATE VACCINE, IS NOW AVAILABLE FROM VFC

SUMMARY

On February 19, 2010, the United States (U.S.) Food and Drug Administration (FDA) licensed a quadrivalent meningococcal conjugate vaccine, Menveo® (Novartis Vaccines and Diagnostics), for use in persons 11 through 55 years of age. This vaccine is indicated for the protection against invasive meningococcal disease caused by the four serogroups (A, C, Y, and W-135). The Advisory Committee on Immunization Practices (ACIP) voted to include Menveo®, along with the currently licensed meningococcal conjugate vaccine, Menactra®, in the VFC program at their February 2010 meeting. The vaccine is now available from VFC for persons 11 through 18 years.

This letter summarizes information about the use of the newly licensed meningococcal conjugate vaccine. The California Department of Public Health, Immunization Branch is following ACIP's recommendations for use of meningococcal conjugate vaccines.

BACKGROUND AND COMPOSITION

Neisseria meningitidis (meningococcus) is a gram-negative diplococcus that causes severe invasive infections such as sepsis and meningitis. The case fatality rate for invasive meningococcal disease is 9-12%, and up to 20% have permanent disability. Meningococci are classified by serogroups based on the polysaccharide capsule. Serogroups A, B, C, Y, and W-135 cause most cases of invasive disease globally. FDA-licensed vaccines (e.g., Menveo® and Menactra®) protect against serogroups A, C, Y, and W-135 but do not protect against serogroup B.

The new vaccine contains *N. meningitidis* serogroups A, C, Y, and W-135 oligosaccharides conjugated individually to CRM_{197} protein, a nontoxic variant of diphtheria toxin. The *N. meningitidis* strains A, C, Y, and W-135 are cultured and grown on Franz Complete media and treated with formaldehyde. The protein carrier is cultured and grown on CY medium containing yeast extracts and amino acids. The final glycoconjugates are then purified.

There are two components to the vaccine:

- 10 mcg of lyophilized meningococcal serogroup A capsular polysaccharide conjugated to CRM_{197} (MenA)
- 5 mcg of each of capsular polysaccharide of serogroup C, Y, and W135 conjugated to CRM_{197} protein in 0.5mL phosphate buffered saline, which is used to reconstitute the lyophilized MenA component before use

The vaccine contains no preservative or adjuvant. The vaccine vials do not contain latex. Residual formaldehyde per dose is estimated to be not more than 0.30 mcg.

Currently the other quadrivalent meningococcal conjugate vaccine, Menactra®, is licensed from ages 2 through 55 years. Menveo® was licensed on its immunologic non-inferiority to Menactra® in both adolescents (11-18 years) and adults (19-55 years) for all four serogroups, based on serum bactericidal assay with human complement (hSBA) seroresponse. The proportion of seroresponders based on hSBA titers was statistically higher in the Menveo® group compared to the Menactra® group for certain serogroups (A, W-135, and Y in adolescents11-18 years and C, W-135, and Y in adults 19-55 years); however, the clinical relevance of this greater immune response is not known.

Since there are now two choices for the meningococcal conjugate vaccine, the CDPH Immunization Branch encourages each provider to review information on both vaccines and to choose one vaccine for use in your practice. It is important to educate all staff regarding the storage, preparation, administration, and recordkeeping for any new vaccine used in your practice.

RECOMMENDATIONS FOR USE OF MENVEO® IN THE VFC PROGRAM

Eligible Persons for Receipt of VFC Supplies

Children ages 2 through 18 years are eligible for meningococcal conjugate vaccines provided by the VFC program. Currently, Menveo® is licensed for those 11-55 years, although only those 11 through 18 years may receive VFC supplies of the vaccine.

Meningococcal Conjugate Vaccine ACIP Recommendations
Meningococcal conjugate vaccines are recommended routinely for all persons aged 11 or 12 years of age. The vaccine is also recommended for those 13 through 18 years if not previously vaccinated.

Meningococcal conjugate vaccine is also recommended for persons aged 2 through 55 years of age who are at increased risk of meningococcal disease. This includes:

- College freshmen living in dormitories
- Microbiologists who are routinely exposed to isolates of *N. meningitidis*
- Military recruits
- Persons who travel to or reside in countries where meningococcal disease is hyperendemic or epidemic
- Persons who have persistent complement component deficiencies
- Persons with anatomic or functional asplenia

Persons infected with HIV are also likely at increased risk of invasive meningococcal disease and may also receive MCV4.

Revaccination is recommended for persons at continued increased risk of meningococcal disease. Persons who

- received meningococcal vaccine at age 7 years or older should be revaccinated 5 years after their previous dose.
- received meningococcal vaccine at ages 2 through 6 years should be revaccinated 3 years after their previous dose.
- remain at increased risk should continue to be revaccinated at 5-year intervals.

College freshmen living in dorms who do not have another risk factor for meningococcal disease are not recommended to be revaccinated with a second dose of meningococcal conjugate vaccine.

Meningococcal conjugate vaccines are preferred to quadrivalent meningococcal polysaccharide vaccine (MPSV4). ACIP recommendations are provided for your information; VFC meningococcal conjugate vaccines are only available for eligible patients ages two years through 18 years.

Administration of Menveo®
Please note that this vaccine requires reconstitution of the vial of lyophilized MenA component with MenCYW-135 liquid component (provided in a separate vial). Using a sterile syringe, the entire contents of the vial of Men CYW-135 liquid conjugate component should be withdrawn and injected into the MenA lyophilized conjugate component vial. The reconstituted vial should be gently inverted or swirled until the vaccine dissolves. After reconstitution, the vaccine should be a clear, colorless solution, without foreign particles. The vaccine should not be administered if particulate matter or discoloration is noted after careful visual inspection. The reconstituted vaccine product should be withdrawn into the syringe and administered by intramuscular injection.

Providers should educate all staff to prevent inadvertent administration of ONLY the liquid component without reconstitution with the lyophilized component.

The lot number written on the Menveo® carton should be documented in the medical record and immunization registry after administration of Menveo®. Providers should be aware that there may be three different lot numbers for Menveo ® (lypophilized vaccine component vial, liquid

vaccine component vial, and the Menveo® carton. Please record the lot number on the carton when documenting Menveo® administration. Please keep vials stored in their original carton to avoid inaccurate recordkeeping.

Administration of Menveo® with other vaccines
Menveo® may be given at the same visit when other age appropriate vaccines are provided, such as Tdap and HPV vaccine. Do not mix this vaccine or any of its components with any other vaccine or diluents in the same syringe or vial. All vaccines should be given at separate sites with separate syringes.

HOW SUPPLIED FOR CALIFORNIA VFC PROGRAM PROVIDERS

Menveo® is supplied as:

- A 5-dose package containing a total of 10 vials.
- Each dose includes:
  - One vial containing the Men CYW-135 liquid component, to be combined with
  - One vial containing MenA lyophilized conjugate

Storage

- Please keep all vials stored in the original carton.
- Menveo® should be refrigerated at 35 - 46 degrees F (2 - 8 degrees C).
- Do not freeze.

POTENTIAL VACCINE REACTIONS

The most common adverse reactions reported were pain at the injection site, headache, and myalgia. Reported adverse reactions were comparable between Menveo® and Menactra®, the previously licensed quadrivalent meningococcal conjugate vaccine.

Syncope can occur after vaccination, most commonly among adolescents and young adults. To avoid serious injury related to a syncopal episode, vaccine providers should consider observing patients for 15 minutes after they are vaccinated. To decrease the risk of injury from syncope, providers should consider having their patients seated during both vaccination and the observation period.

Providers should report suspected reactions to meningococcal conjugate vaccines or any other vaccine to the Vaccine Adverse Events Reporting System (VAERS) at 800-822-7967 (toll-free) or http://vaers.hhs.gov.

CONTRAINDICATIONS

- History of severe allergic reaction (e.g., anaphylaxis) after a previous dose of any CRM_{197}, diphtheria toxoid, or meningococcal-containing vaccine or any other component of the vaccine.

PRECAUTIONS

- Meningococcal conjugate vaccines can be administered to persons with minor acute illnesses (e.g., diarrhea or mild upper respiratory tract infections, with or without fever).
- Vaccination of people with moderate or severe acute illnesses should be deferred until after the illness improves.

USE DURING PREGNANCY

- Pregnancy is not a contraindication to use of meningococcal conjugate vaccines; however, no clinical trials have specifically been conducted to assess the use of meningococcal conjugate vaccines during pregnancy.
- Any exposure to Menveo® vaccine during pregnancy should be reported to the manufacturer's vaccine pregnancy registry so that the manufacturer may collect additional data on its use in pregnant women.
  - Novartis Vaccines and Diagnostics, Inc. (*Menveo®)* 1-877-311-8972.

ORDERING AND BILLING

How to Order

The VFC Order Form, [DHS 8501 (04/10)] has been revised to include this new product under the "Meningococcal" vaccine section. Providers may request doses of this product using the revised order form (attached). Doses requested should be included with routine vaccine requests. Remember to complete all the boxes in the four columns of the order form. Maintain a copy of your order forms for your office files. Please be aware that your orders of the Menveo® vaccine may be adjusted, especially during this introductory phase.

Requests for this product should be based on your clinic's meningococcal vaccine usage and current inventory on hand. When transitioning to a new product brand or presentation, inventory of currently used product should be decreased to prevent any unnecessary vaccine wastage or product confusion as the new product is received.

Billing Information for VFC Meningococcal Conjugate Vaccines

CHDP: The CHDP administration fee is $9.00 using CHDP code 69 for doses of the meningococcal conjugate vaccine administered to children 2 years through the age of 18 years enrolled in the CHDP Program. A high risk factor is required for children younger than 11 years who receive meningococcal conjugate vaccines licensed for this age group. CHDP Provider Information Notices can be found at http://www.dhcs.ca.gov/formsandpubs/publications/Pages/CMSLetters.aspx.

Medi-Cal Fee-For-Service (FFS):

Medi-Cal billing codes for administration of Menveo® have not yet been published. However, once these codes are published in the Medi-Cal Provider Bulletin, providers may then bill for administration of this vaccine provided by the VFC program. Services are only considered benefits of the Medi-Cal Program once published in the Provider Bulletins at http://files.medi-cal.ca.gov/pubsdoco/Bulletins_menu.asp. Providers should check the Medi-Cal provider manual for final codes and implementation date(s). The provider manual can be downloaded at: http://files.medi-cal.ca.gov/pubsdoco/publications/masters-mtp/part2/vaccine_m00o03o04o11.doc.

Other codes for Menveo® vaccine that is not supplied by VFC:

- The CPT code for meningococcal conjugate vaccine is **90734**.
- The ICD-9-CM code for the need for prophylactic vaccination against a specified bacterial disease **V03.89**.
- NDC Code: **46028-208-01**

DOCUMENTATION - HYPERLINKS

1) ACIP recommendations:

- Licensure of a Meningococcal Conjugate Vaccine (Menveo®) and Guidance for Use--- Advisory Committee of Immunization Practices (ACIP). MMWR, 2010. 59(09).
- Updated Recommendation from the ACIP for Revaccination of Persons at Prolonged Increased Risk for Meningococcal Disease. MMWR 2008; 58(37).
- Recommendation from the ACIP for Use of MCV4 in Children Aged 2--10 Years at Increased Risk for Invasive Meningococcal Disease. MMWR, 2007; 56(48).

2) Product Inserts:

- Menveo®
- Menactra®

3) Vaccine Information Statement (VIS) for meningococcal conjugate vaccines

4) AAP recommendations (members-only): http://www.cispimmunize.org/

5) VFC resolution No. 06/09-2 on meningococcal conjugate vaccines

6) Vaccine Injury Compensation Program (VICP): Meningococcal conjugate vaccines are covered by the federal VICP .

Enclosures: Order Form (04/10) http://www.eziz.org/PDF/CDPH-8501.pdf

cc: CDPH Immunization Branch Field Representatives
Local Health Officers
Local Health Department Immunization Coordinators
Local Health Department CHDP Program Directors
Tanya Homman, Acting Chief, Medi-Cal Managed Care Division, DHCS
Luis Rico., Acting Chief, Children Medical Services Branch, DHCS
Susan McClair, M.D., Acting Chief, Medical Policy, Medi-Cal Managed Care, DHCS
Shabbir Ahmad, D.V.M., M.S., Ph.D., Acting Chief, Maternal, Child and Adolescent Health Program, CDPH
Shelley Rouillard, Deputy Director, Benefits and Quality Monitoring Division, MRMIB
Lilia Coleman, Benefits and Quality Monitoring, MRMIB
Jamie Yang, Benefits and Quality Monitoring, MRMIB
Neal Kohatsu, M.D., M.P.H., Medical Policy Section, Medi-Cal Benefits, Waiver Analysis and Rates Division, DHCS
Steve Shih, M.D. Medical Policy Section, Medi-Cal Benefits, Waiver Analysis and Rates Division, DHCS
Laura Ann Halliday, M.D. Medical Policy Section, Medi-Cal Benefits, Waiver Analysis and Rates Division, DHCS
Alan Morita, Pharm.D., Medi-Cal Pharmacy Policy Branch, DHCS
Jill Abramson, M.D., M.P.H., Children Medical Services Branch, DHCS
Neal Kohastu, M.D., M.P.H., Medical Policy Section, Medi-Cal Benefits, Waiver Analysis and Rates Division, DHCS
Steve Shih, M.D. Medical Policy Section, Medi-Cal Benefits, Waiver Analysis and Rates Division, DHCS
Alan Morita, Pharm.D., Medi-Cal Pharmacy Policy Branch, DHCS
Jill Abramson, M.D., M.P.H., Children Medical Services Branch, DHCS