Recommendation of the Advisory Committee on Immunization Practices (ACIP) for Use of Quadrivalent Meningococcal Conjugate Vaccine (MenACWY-D) Among Children Aged 9 Through 23 Months at Increased Risk for Invasive Meningococcal Disease

In April 2011, the Food and Drug Administration approved the use of a quadrivalent meningococcal conjugate vaccine (MenACWY-D) (Menactra, Sanofi Pasteur) as a 2-dose primary series among children aged 9 through 23 months (*1*). Vaccination with meningococcal polysaccharide vaccine (MPSV4) is not recommended for children aged <2 years because of low immunogenicity and short duration of protection in this age group (*2*).

The Advisory Committee on Immunization Practices (ACIP) Meningococcal Vaccine Work Group reviewed data from four clinical studies on the safety and immunogenicity of MenACWY-D in healthy children aged 9 through 23 months. The pivotal immunogenicity study was a Phase III, multicenter, U.S. trial measuring seroresponse 30 days after 2 doses of MenACWY-D. Antibody titers were measured using a serum bactericidal assay containing human complement (hSBA). Seroresponse was defined as the proportion of subjects with hSBA titers of ≥1:8, the accepted measure of protection. The first dose of MenACWY-D was administered alone at age 9 months, followed by a second dose administered alone (n = 404) or concomitantly with measles, mumps, rubella, and varicella vaccine (n = 302) or 7-valent pneumococcal conjugate vaccine (PCV7) (n = 422) at age 12 months. The percentage of subjects with hSBA titers ≥1:8 was >90% for all meningococcal serogroups except serogroup W135 (>80%) (*3*).

Immune responses to childhood vaccines recommended by ACIP at age 12 months, administered concomitantly with MenACWY-D, were evaluated in a separate randomized, multicenter, U.S. trial. After coadministration of MenACWY-D and PCV7, lower geometric mean concentrations (GMCs) of antipneumococcal immunoglobulin G (IgG) were observed compared with corresponding IgG GMCs when PCV7 was administered without MenACWY-D. The noninferiority criteria (twofold differences in IgG GMCs) for the prespecified pneumococcal endpoints were not met for serotypes 4, 6B, and 18C (*3*). However, the IgG antibody responses to the seven pneumococcal vaccine serotypes were still robust. For an individual, the clinical relevance of decreased pneumococcal antibody responses to three of seven vaccine serotypes is not known. No data are available on the immune responses to coadministered MenACWY-D and a CRM197-based 13-valent pneumococcal conjugate vaccine (PCV13). The most common solicited adverse events for MenACWY-D included injection site tenderness and irritability; no serious adverse events were attributed to MenACWY-D (*3*).

Antibody persistence and response to a MenACWY-D booster dose was evaluated among 60 subjects who received 2 doses of MenACWY-D as part of a Phase II clinical study (*4*). hSBA titers were measured approximately 3 years after dose 2, which was administered at either 12 or 15 months of age. Before receiving a booster dose, <50% of subjects had maintained hSBA titers ≥1:8 for any of the meningococcal serogroups. After booster immunization, ≥98% of subjects had hSBA titers ≥1:8 to each of the serogroups.

After review of these clinical data at the June 2011 meeting, ACIP recommended that children aged 9 through 23 months with certain risk factors for meningococcal disease receive a 2-dose series of MenACWY-D, 3 months apart. This includes children who have persistent complement component deficiencies (e.g., C5–C9, properdin, factor H, or factor D), children who are traveling to or residents of countries where meningococcal disease is hyperendemic or epidemic, and children who are in a defined risk group during a community or institutional meningococcal outbreak (*2*). Because of their high risk for invasive pneumococcal disease, children with functional or anatomic asplenia should be vaccinated with MenACWY-D beginning at age 2 years to avoid interference with the immunologic response to the infant series of PCV. If children aged ≥2 years with functional or anatomic asplenia have not yet received all recommended doses of PCV, they should receive all recommended doses separated from MenACWY-D by at least 4 weeks.

A 2-dose primary series is required for any child with the risk factors described in this report whose first dose was received before their second birthday. If dose 2 was not received on schedule (3 months after dose 1), it should be administered at the next available opportunity. The minimum interval between doses is 8 weeks. Children who received the 2-dose series at age 9 through 23 months and are at prolonged, increased risk should receive a booster 3 years after completing the primary series. After this initial booster, persons who remain in one of the increased risk groups should continue to receive a booster dose at 5-year intervals (Table). Recommendations for use of MenACWY-D among persons aged 2 through 55 years have been published previously and remain unchanged (*2,5,6*).

TABLE. Summary of MenACWY-D recommendations for children aged 9 through 23 months at high risk for invasive meningococcal disease — Advisory Committee on Immunization Practices (ACIP)

Risk group	Primary series	Booster dose
Children aged 9 through 23 months at high risk for invasive meningococcal disease (except children with functional or anatomic asplenia)*	2 doses, 3 months apart	Initial booster 3 years after completing the primary series†
	Catch-up dose if dose 2 is not received on schedule: at the earliest opportunity	Continued boosters at 5-year intervals after the initial booster†
Children at high risk for invasive meningococcal disease with functional or anatomic asplenia	2 doses, 2 months apart, beginning at age 2 years and ≥4 weeks after completion of PCV13 vaccine series	Initial booster 3 years after completing the primary series†
		Continued boosters at 5-year intervals after the initial booster†

Abbreviations: MenACWY-D = quadrivalent meningococcal conjugate vaccine; PCV13 = 13-valent pneumococcal conjugate vaccine.

* Children who have persistent complement component deficiencies (e.g., C5–C9, properdin, factor H, or factor D), children who are traveling to or residents of countries where meningococcal disease is hyperendemic or epidemic, and children who are in a defined risk group during a community or institutional meningococcal outbreak.

† If the person remains at increased risk.

References

1. Food and Drug Administration. April 22, 2011 approval letter—Menactra. Silver Spring, MD: US Department of Health and Human Services, Food and Drug Administration; 2011. Available at http://www.fda.gov/biologicsbloodvaccines/vaccines/approvedproducts/ucm252511.htm. Accessed October 4, 2011.
2. CDC. Prevention and control of meningococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2005;54(No. RR-7).
3. Food and Drug Administration. Product approval information: package insert. Menactra (meningococcal (groups A, C, Y and W-135) polysaccharide diphtheria toxoid conjugate vaccine). Sanofi Pasteur. Silver Spring, MD: US Department of Health and Human Services, Food and Drug Administration; 2011. Available at http://www.fda.gov/downloads/biologicsbloodvaccines/vaccines/approvedproducts/ucm131170.pdf. Accessed October 4, 2011.
4. Johnson DR. Menactra infant indication; meningococcal (groups A, C, Y and W-135) polysaccharide diphtheria toxoid conjugate vaccine. Presented at the meeting of the Advisory Committee on Immunization Practices, Atlanta, GA, June 22, 2011.
5. CDC. 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 2007;56:1265–6.
6. CDC. Updated recommendation from the Advisory Committee on Immunization Practices (ACIP) for revaccination of persons at prolonged increased risk for meningococcal disease. MMWR 2009;58:1042–3.