Licensure of 13-Valent Pneumococcal Conjugate Vaccine for Adults Aged 50 Years and Older

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In 2010, 13-valent pneumococcal conjugate vaccine (PCV13 [Prevnar 13, Wyeth Pharmaceuticals, Inc., a subsidiary of Pfizer, Inc.]) was licensed by the Food and Drug Administration (FDA) and recommended by the Advisory Committee on Immunization Practices (ACIP) for children aged 6 weeks through 71 months for the prevention of invasive pneumococcal disease (IPD) caused by the 13 pneumococcal serotypes included in the vaccine. PCV13 currently is recommended as a 4-dose series for children starting at age 2 months. On December 30, 2011, FDA approved PCV13 for prevention of pneumonia and invasive disease caused by PCV13 serotypes among adults aged 50 years and older. This report summarizes data on the immunogenicity and safety of PCV13 in adults and outlines key additional evidence requested by ACIP to formulate recommendations for its use.

FDA approved PCV13 for an adult indication under the Accelerated Approval pathway, which allows the agency to approve products for serious or life-threatening diseases on the basis of early evidence of a product's effectiveness that is "reasonably likely to predict clinical benefit" (1). Approval of PCV13 for adults was based on immunogenicity studies that compared antibody responses to PCV13 with antibody responses to 23-valent pneumococcal polysaccharide vaccine (PPSV23, [Pneumovax 23, Merck, Inc.]), a vaccine that provides protection against IPD but for which no consensus exists regarding protection against nonbacteremic pneumococcal pneumonia (2). Of note, the level of vaccine-induced pneumococcal antibody in adults that correlates with protection against clinical disease, including IPD or pneumococcal pneumonia, has not been established.

In two randomized, multicenter, immunogenicity studies conducted in the United States and Europe, adults aged 50 years and older received a single dose of PCV13 or PPSV23 (3). Functional antibody responses were measured 1 month after vaccination using an opsonophagocytic activity (OPA) assay. In adults aged 60 through 64 years, PCV13 elicited OPA geometric mean antibody titers (GMTs) to the 12 serotypes common to both vaccines that were comparable to, or higher than, responses elicited by PPSV23. For serotype 6A, which is unique to PCV13, OPA antibody responses were higher after PCV13 vaccination than after PPSV23 vaccination. OPA GMTs elicited by PCV13 in adults aged 50 through 59 years for all 13 serotypes were comparable to the corresponding GMTs elicited by administration of PCV13 in adults aged 60 through 64 years. In adults aged 70 years and older who previously had been immunized with a single dose of PPSV23 at least 5 years before enrollment, PCV13 elicited OPA responses that were comparable to or higher than those elicited by PPSV23 for the 13 serotypes. For 10 of 12 serotypes in common, the PCV13 responses were significantly greater than the PPSV23 responses. At 1-year follow up, OPA levels were lower in PCV13 and in PPSV23 recipients than at 1 month. An evaluation of responses after a second pneumococcal vaccination administered 1 year after the initial study doses showed that a second dose of PCV13 generally resulted in OPA levels similar to those observed after the first dose. In contrast, subjects who received PPSV23 as the initial study dose had lower OPA antibody responses after subsequent administration of PCV13 than those who had received PCV13 as the initial dose, regardless of the level of the initial OPA response to PPSV23 (3).

Safety of PCV13 was evaluated in approximately 6,000 PPSV23-naïve and PPSV23-experienced adults aged 50 years and older (3). Overall incidence of serious adverse events reported within 1 month of an initial study dose of PCV13 or PPSV23 ranged from 0.2% to 1.7%. From 1 month to 6 months after an initial study dose, the overall

incidence of serious adverse events ranged from 1.2% to 5.8% among persons vaccinated with PCV13 and 2.4% to 5.5% among persons vaccinated with PPSV23. Rates of serious adverse events reported between the treatment groups were similar among studies that enrolled PPSV23-naïve subjects and studies that enrolled PPSV23-experienced subjects. Common adverse reactions reported with PCV13 were pain, redness, and swelling at the injection site; limitation of movement of the injected arm; fatigue; headache; chills; decreased appetite; generalized muscle pain; and joint pain. Similar reactions were observed in adults who received PPSV23.

At the February and June 2011 meetings of ACIP, published and unpublished data were presented on the epidemiology of pneumococcal disease and PCV13 safety and immunogenicity (4). Two critical gaps in evidence needed to support a recommendation for routine PCV13 use among adults were identified. First, no available data demonstrated clinical efficacy of PCV13 against pneumococcal pneumonia in adults. As part of FDA's accelerated approval process, the manufacturer has agreed to conduct further studies to verify the anticipated benefit of the vaccine (1). To this end, a trial in 85,000 persons aged 65 years and older who have never received PPSV23 is under way in the Netherlands to assess the clinical benefit of PCV13 in the prevention of pneumococcal pneumonia (5). Second, the full impact of routine PCV13 vaccination among children on the incidence of pneumococcal disease caused by PCV13 serotypes in adults is not known at this time. Substantial reductions in incidence of pneumococcal disease caused by serotypes in the 7-valent pneumococcal conjugate vaccine (PCV7 [Prevnar, Wyeth]) were noted among adults after routine vaccination of children with PCV7 began in 2000 (6). PCV13 serotypes currently account for approximately one third of IPD among adults aged 65 years and older (CDC, unpublished data, 2010). In addition, 11 serotypes that account for 25% of IPD in adults aged 65 years and older are included in PPSV23 but not in PCV13. If indirect effects of similar magnitude to that of PCV7 are observed from the introduction of PCV13 in 2010, the potential benefit of vaccinating adults with PCV13 is likely to be reduced substantially. National surveillance systems monitoring pneumococcal infections are tracking the impact of the pediatric PCV13 program and will measure the magnitude of indirect effects on adults. The results of the clinical trial in the Netherlands and the extent of indirect effects of the infant PCV13 program will provide critical information that will help guide ACIP deliberations regarding routine PCV13 use among adults aged 50 years and older; both pieces of information are expected to be available in 2013.

At this time, two vaccines for prevention of pneumococcal disease are licensed for use in adults. ACIP currently recommends a single dose of PPSV23 for all persons aged 65 years and older. In addition, for adults aged 19 through 64 years, PPSV23 should be administered to those with immunocompromising conditions (including chronic renal failure or nephrotic syndrome); those with functional or anatomic asplenia; those who are immunocompetent and have chronic conditions such as alcoholism, diabetes mellitus, or chronic lung disease; those who are smokers; and those with cochlear implants or cerebrospinal fluid leaks (2). Adults who received PPSV23 before age 65 years for any indication should receive another dose of the vaccine at age 65 years or later if at least 5 years have passed since their previous dose. A second dose of PPSV23 is recommended 5 years after the first dose for persons aged 19 through 64 years with functional or anatomic asplenia and for persons with immunocompromising conditions. ACIP does not recommend routine revaccinations with PPSV23 because of insufficient data regarding clinical benefit, particularly the degree and duration of protection, and safety (2). Although not yet recommended by ACIP, PCV13 is available for use among adults aged 50 years and older in accordance with the package insert.

ACIP will continue to review evidence as it becomes available to guide development of a recommendation regarding routine use of PCV13 in adults aged 50 years and older. In the meantime, health-care providers should continue to administer PPSV23 in accordance with current recommendations. According to recent data, at least one third of persons aged 65 years and older have not received the recommended dose of PPSV23, indicating a need to continue to improve vaccination coverage in this population (7). At the June 2012 meeting, ACIP will discuss available evidence regarding administration of PCV13 to adults with immunocompromising conditions who are at high risk for developing pneumococcal disease.

References

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