13-Valent PCV Poised to Replace 7-Valent Version

BY MIRIAM E. TUCKER

ATLANTA — Wyeth Pharmaceuticals is in the process of planning the transition from routine childhood immunization with the 7-valent Prevnar to use of a 13-valent pneumococcal conjugate vaccine that is still under investigation.

The Food and Drug Administration has granted fast-track status for PCV13 for the pediatric indication, based on "an unmet medical need." The company plans to complete the data submission process for PCV13 by the end of this month, at which point the agency will decide about priority review, Peter Paradiso, Ph.D., vice president of new business and scientific affairs at Wyeth Pharmaceuticals, Collegeville, Pa., said at the winter meeting of the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention.

"Our goal is that PCV13 will replace PCV7," he said.

The 13-valent version contains the same amounts of the same seven serotypes that Prevnar has (4, 6B, 9V, 14, 18C, 19F, and 23F) along with six new strains (1, 3, 5, 6A, 7F, and 19A). Each of these polysaccharides in both vaccines is conjugated to the same carrier protein, CRM197, using the same conjugation chemistry. "So, PCV13 uses a technology that has worked successfully with Prevnar," he noted.

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"So, PCV13 uses a technology that has worked successfully with Prevnar," Peter Paradiso, Ph.D., of Wyeth Pharmaceuticals, said.

Since the introduction of Prevnar in 2000, the proportion of cases of invasive pneumococcal disease (IPD) caused by the seven vaccine strains has declined dramatically, while the proportion due to other strains—19A in particular—has risen. In 2006, the proportion of IPD cases caused by the seven strains included in Prevnar was 2% in children aged younger than 2 years and 4% in those aged 2-4 years. In contrast, the proportion of IPD cases caused by the 13 serotypes in the new version was 64% and 73%, respectively, with half of the cases due to 19A.

Dr. Paradiso summarized previously reported data from a pivotal trial done in Germany in which 603 infants were randomized to receive either PCV7 or PCV13 at 2, 3, and 4 months of age. The 13-valent version was noninferior against each serotype, while provoking a high antibody response rate to each of the six new serotypes. The overall safety profile of PCV13 was comparable with that of PCV7 in a database that includes 4,783 PCV13 recipients in a total study population of 7,240, he said.

Wyeth's transition scheme—which would be subject to approval by both the FDA and the ACIP after PCV13 is licensed—would involve the substitution of PCV13 for PCV7 at any point in the immunization schedule.

Because data have shown that a single dose of PCV13 will induce an immune response to the six new serotypes in more than 90% of children aged 12 months and older, any child who received the primary three-dose series with PCV7 could simply receive PCV13 as a booster after they reach the age of 12 months. For children 12 months and older who already received the complete series with PCV7 including the booster, one additional dose of PCV13 would be needed for protection against the six new strains. Infants aged 6 months or younger who received one or two doses of PCV7 would complete the primary series and the booster using PCV13.

In January, Wyeth initiated a study in the Yukon-Kuskokwim Delta region of Alaska to test the safety and effectiveness of this scheme in children younger than 5 years old, he said.

The company will first seek an indication for the use of PCV13 in children younger than 5 years old. After that, it hopes to bring it to adults over age 50, and ultimately to the entire population. "Our goal is to fill in the gaps and make this vaccine available for all age groups," Dr. Paradiso said.

In response to an audience member's query as to whether PCV13 would cost more than PCV7, Dr. Paradiso replied, "I honestly don't know the answer to that question. Obviously, that's something you'll hear about as we get closer [to implementation]." ■

FDA Panel Votes on the Strains for the Next Flu Vaccine

BY ELIZABETH MECHCATIE

SILVER SPRING, MD. — The influenza B strain in the current influenza vaccine in the United States should be replaced for the 2009-2010 influenza vaccine, according to a preliminary recommendation by a federal advisory panel, which based its decision on data on circulating viruses collected to date during this influenza season.

At a Feb. 18 meeting, the Food and Drug Administration's Vaccines and Related Biological Products Advisory Committee voted in favor of replacing the current B component of the vaccine, a B/Florida/4/2006–like virus (a B/Yamagata lineage virus), with a B/Brisbane/60/2008–like virus (a B/Victoria lineage virus).

The panelists unanimously voted to retain the two influenza A strains included in the current vaccine for the next season's vaccine. The influenza A (H1N1) strain in the current vaccine is an A/Brisbane/59/2007–like virus; the H3N2 strain is an A/Brisbane/10/2007–like virus. The panel's recommendations are not final; they will meet again to discuss the final recommendations later in the influenza season, taking into account data collected on influenza virus activity for the remainder of the season.

The panel's recommendations concur with those of the World Health Organization to retain the two influenza A strains, but to change the B strain to a B/Brisbane/60/2008–like virus, which reflects the B virus that is predominant worldwide.

On Feb. 24, the vaccine's use was endorsed for the upcoming influenza season by the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention. The ACIP did not recommend any new age or risk groups be added to the list of those recommended to receive the vaccine, which currently includes 84% of the U.S. population. The remaining individuals—healthy adults aged 19-49 who are not close contacts of a child or other high-risk individual—are covered under the permissive recommendation for vaccination of "all individuals who want to reduce the risk of becoming ill with influenza or of transmitting it to others," Dr. Anthony Fiore, of the CDC's influenza division, said at the ACIP meeting.

The ACIP did vote for some minor changes to its annual influenza statement, including removing the provisional "if feasible" phrase from the recommendation to vaccinate all children aged 6 months through 18 years and adding additional background information in support of vaccinating pregnant women and for routine vaccination of persons with vaccine indications during hospitalization. The ACIP also discussed the addition of information about ocular and respiratory symptoms following receipt of the injectable influenza vaccine (seen in less than 6% of recipients) to the statement's safety section, but postponed a vote on including that information until June, when more data are expected to be available.

At the FDA hearing, Alexander Klimov, Ph.D., noted that there are two major circulating lineages of influenza B viruses, Victoria and Yamagata. Worldwide, B viruses of both lineages (B/Victoria/2/87 and B/Yamagata/16/88 viruses) have cocirculated with H1N1 or H3N2 viruses, according to Dr. Klimov, chief of the virus surveillance and diagnosis branch, in the Centers for Disease Control and Prevention's influenza division. However, more than 60% of circulating B viruses are from B Victoria lineage, he said at the meeting.

During this season to date, influenza A (H1N1) viruses have predominated in the United States and in many other North American countries and in Asian countries, and the majority of the viruses have been closely related to the H1N1 strain included in the current vaccine, said Dr. Klimov, who is also deputy director of the WHO Collaborating Center for Surveillance, Epidemiology, and Control of Influenza.

Influenza A (H3N2) viruses have been cocirculating with H1N1 and B viruses in many countries, predominantly in most European countries and in Japan. Most have been antigenically similar to the H3N2 strain in the current vaccine, and have been sensitive to the influenza antivirals oseltamivir (Tamiflu) and zanamivir (Relenza), Dr. Klimov said.

In the United States, oseltamivir-resistant influenza A (H1N1) has predominated this season and has been found in 30 states, said Dr. Joseph Bresee of the epidemiology and prevention branch, in the CDC's influenza division. Oseltamivir-resistant H1N1 strains were antigenically similar or identical to the strains in the current vaccine. Viruses that have been sensitive to and those resistant to oseltamivir have been antigenically similar, he added.

This was the topic of a health advisory issued by the CDC in December, which recommended that zanamivir or a combination of oseltamivir and rimantadine (Flumadine) are more appropriate options than oseltamivir alone when influenza A (H1N1) virus infection or exposure is suspected. ■