13-Valent PCV Poised To Replace 7-Valent

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 planned to complete the data submission process for PCV13 by the end of March, at which point the agency would decide about priority review, Peter Paradiso, Ph.D., vice president of new business and scientific affairs at Wyeth, Collegeville, Pa., said at the winter meeting of the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention.

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, he noted.

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 caused by other strains—19A in particular—has risen.

Dr. Paradiso summarized previously reported data from a pivotal trial done in Germany in which 603 infants received 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.

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.

Since data show 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 3-dose series with PCV7 could simply receive PCV13 as a booster after 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. Infants aged 6 months or younger who received one or two doses of PCV7 would complete the primary series and the booster using PCV13.

The company will first seek an indication for the use of PCV13 in children under 5 years old. It then hopes to bring it to adults over age 50, and ultimately to the entire population, Dr. Paradiso said. ■

Infanrix Insert Updated With More Safety Data

More safety information has been added to the package insert for Infanrix, the Food and Drug Administration said.

The insert now includes the statement that Infanrix (Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed) "may be used to complete a DTaP vaccination series initiated" with Pediarix (Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed, Hepatitis B [Recombinant] and Inactivated Poliovirus Vaccine Combined), because both vaccines use the same pertussis antigen components, according to a statement issued by the FDA.

Infanrix is administered as a five-dose series at 2, 4, and 6 months, with booster doses at 15-20 months and at 4-6 years. Both vaccines are marketed by GlaxoSmithKline Biologicals. Pediarix is recommended as a three-dose primary series, starting as early as 6 weeks of age.

Also added were data on safety and immune responses on the concomitant administration of Infanrix with other vaccines.

The information was added when the insert was revised to conform with guidelines outlined in the FDA's Physician Labeling Rule, according to a GSK spokesperson. The rule requires that the package inserts of approved products be reordered and reorganized into a more user-friendly format.

—Elizabeth Mechcatie

The updated Infanrix insert is available at www.fda.gov/cber/label/infanrixLB.pdf.

CLINICAL GUIDELINES FOR FAMILY PHYSICIANS

AHA: Streptococcal Pharyngitis

BY NEIL SKOLNIK, M.D., AND MATHEW CLARK, M.D.

Pharyngitis is one of the more common acute illnesses seen in primary care. In spite of this, the most appropriate approach to diagnosis and treatment of pharyngitis remains controversial, with various organizations promulgating guidelines that reflect differences in interpretation of knowledge and differences in the weighing of competing priorities. Guidelines recently released by the American Heart Association update recommendations from 1995 (Circulation 2009;119:1541-51).

Guidelines are most useful when they are available at the point of care. A free and concise handheld computer version of this guideline is available for download at www.redi-reference.com.

The majority of cases of acute pharyngitis have a viral etiology. This is true for children, adolescents, and especially adults, where the proportion of viral pharyngitis exceeds 90%. Nevertheless, a major clinical priority has been to identify those cases of pharyngitis that are caused by acute infection with group A beta-hemolytic streptococcal (GAS) infection, and to treat infected patients with appropriate antibiotics. It is hard to distinguish pharyngitis caused by GAS from viral pharyngitis on clinical grounds alone; laboratory confirmation is usually necessary to accurately make the diagnosis.

There are several reasons to identify and treat GAS. One goal is to relieve acute symptoms. However, acute GAS tonsillitis is usually a self-limited condition, and antibiotic treatment has only a modest clinical effect, shortening symptoms by roughly 16 hours if begun within the first 3 days of illness. A second goal is to prevent suppurative complications of acute GAS infection, including peritonsillar abscess. Because such complications are rare, this is also a goal of small to modest priority.

Providers may want to treat acute GAS pharyngitis in order to prevent the development of acute rheumatic fever. This is a major potential complication, particularly if it leads to associated cardiac involvement, including valvular disease, and is the reason the American Heart Association was involved in creating these guidelines. It is unclear, however, just how great a risk rheumatic fever currently poses in the United States. In the last several decades, the incidence of acute rheumatic fever following GAS pharyngitis has been very low in children, and practically nonexistent in older adults.

Counterbalancing these reasons for identifying and treating GAS pharyngitis are increasing concerns about the overuse of antibiotics, with the attendant risks of adverse reactions and the emergence of widespread antibiotic resistance.

Clinical and epidemiological features that suggest GAS as a causative agent of acute pharyngitis include sudden onset; pain on swallowing; fever; scarlet fever rash; headache; nausea; abdominal pain; tonsillopharyngeal erythema or exudates; palatal petechiae; a beefy, red, swollen uvula; tender, enlarged anterior cervical nodes; ages 5-15 years; presentation in winter or early spring; and a history of exposure.

Features that suggest a viral origin include conjunctivitis, coryza, hoarseness, cough, diarrhea, exanthems, or enanthems.

In patients whose picture strongly suggests a viral etiology, neither testing nor antibiotic treatment is indicated. In those whose symptoms may be caused by GAS, they recommend laboratory testing, with either a rapid antigen-detection test (RADT) or a throat culture, reserving antibiotic treatment for those patients with proven streptococcal infection. RADTs are quite specific so that a positive test can be trusted as a basis for antibiotic treatment. However, RADTs have historically lacked sensitivity so that negative tests require follow-up throat cultures for greater diagnostic certainty. Newer tests, however, have significantly improved sensitivity that may approach that of a throat culture.

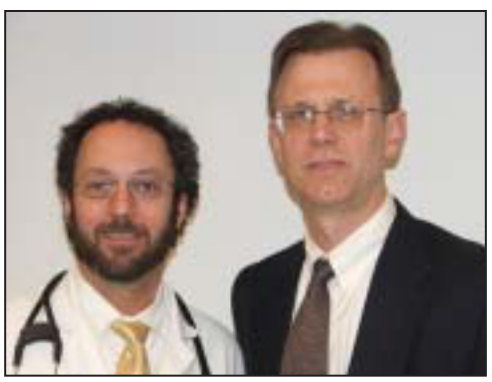
The AHA states that in adults, where GAS is relatively uncommon and the risk of rheumatic fever is extremely small, a negative RADT does not require confirmation. In children, however, they continue to advise follow-up throat cultures for all patients with negative RADTs.

Once GAS infection is confirmed, the AHA recommends treatment with oral or intramuscular penicillin or amoxicillin for 10 days. Alternatives for penicillin-allergic patients include macrolides, oral first-generation cephalosporins, and oral clindamycin.

The Bottom Line

Patients whose picture suggests a viral etiology of their pharyngitis do not need testing and should not receive antibiotics. Patients with features suggestive of GAS infection should be tested. A positive RADT is specific enough to warrant treatment with antibiotics. Negative RADTs are sufficiently accurate in adults, but should be confirmed with follow-up throat cultures in children and adolescents.

Patients with confirmed GAS pharyngitis should receive intramuscular penicillin or 10 days of oral penicillin or amoxicillin. Alternatives for penicillin-allergic patients include macrolides, first-generation cephalosporins, or clindamycin.



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