Safety of Herpes Zoster Vaccine Affirmed at 1 Year

BY HEIDI SPLETE
Senior Writer

ATLANTA — The safety profile for herpes zoster vaccine Zostavax, manufactured by Merck & Co., was reinforced during its first year of widespread use, based on adverse event reports collected from clinicians, patients, and others.

"Zostavax seems to have a very good safety profile, which was expected based on data from prelicensure trials," said Dr. Sandra Chaves of the Centers for Disease Control and Prevention's Division of Viral and Rickettsial Disease.

A total of 590 reports related to Zostavax (including 44 classified as serious) had been submitted as of June 1, 2007, to the Vaccine Adverse Event Reporting System (VAERS), a vaccine safety surveillance system operated by the CDC and the Food and Drug Administration. The overall reporting rate was 73.3/100,000 doses distributed, and the serious event reporting rate was 5.5/100,000 doses distributed. Two of the 44 serious events reported were deaths. Most (90%) of the reports referred to the Zostavax vaccine administered alone, and 82 reports involved possible off-label use or medical error.

Serious events were defined as instances of hospitalization, death, life-threatening conditions, disabling illness, or other medically important conditions, said Dr. Chaves, who presented the VAERS postlicensure safety data at the late June meeting of the CDC's Advisory Committee on Immunization Practices (ACIP). The herpes zoster vaccine was first licensed in May 2006 and recommended by ACIP for prevention of herpes zoster in adults aged 60 years and older in October 2006.

An injection site reaction—the most commonly reported adverse event—was reported in 307 cases. The next most frequent events were a rash (177 cases) and herpes zoster (145 cases). Some reports included more than one event.

The rate of serious adverse events was higher among vaccine recipients, compared with those who received a placebo, in an adverse event monitoring substudy of approximately 6,000 patients, but no specific pattern was observed, Dr. Chaves said.

More than half (59%) of the 44 serious events occurred in women, and most (43%) occurred in patients aged 70-79 years.

Examples of nonfatal events included three cases of anaphylaxis in patients aged 71, 76, and 79 years, all of whom recovered fully, and one case of a woman who requested vaccination and discovered 10 days later that she was pregnant. No pregnancy outcome data are available, but the woman was being followed by the Pregnancy Registry for Varicella Zoster Virus–Containing Vaccines sponsored by Merck.

The two deaths that occurred within 6 months of vaccination occurred in female patients aged 80 and 83 years, who died from a heart attack and pneumonia with sepsis, respectively.

In addition, administration errors were reported in both adults and children, including 34 reports of Zostavax being given to children instead of Varivax, Merck's childhood varicella vaccine. The adverse event reports suggest that the errors were simply human error and not caused by confusing medication labels, Dr. Chaves said.

One of the committee members expressed concern about the outcomes in children who received Zostavax instead of the children's varicella vaccine. Each dose of Zostavax contains 14 times the amount of varicella zoster virus as Varivax.

A Merck spokesperson who was present at the meeting said that the company had studied titers as high as 50,000 plaque-forming units in healthy children and found a plateau of response, so an accidental dose of Zostavax should not be dangerous in most cases and should not prevent a second dose of varicella vaccine in children who received Zostavax accidentally as the first dose.

Safety surveillance for the zoster vaccine is challenging because of the many comorbid conditions in the 60-years-and-older population, Dr. Chaves noted.

"More data are needed and postlicensure safety studies are expected, which will add to the information on the safety profile of this vaccine," Dr. Chaves said. Merck has agreed to conduct postlicensure studies including a randomized, placebo-controlled safety study with up to 6 months' follow-up to assess the rates of serious adverse events further. ■

ACIP Stresses Value of Influenza Vaccine for Medical Personnel

BY HEIDI SPLETE
Senior Writer

The Centers for Disease Control and Prevention's updated recommendations for the 2007-2008 flu season emphasize vaccinating health care personnel and catching up previously unvaccinated children aged 6 months to 8 years with two doses of vaccine.

The CDC's Advisory Committee on Immunization Practices (ACIP) published its updated flu vaccination recommendations for the 2007-2008 flu season in the July 13 issue of the Morbidity and Mortality Weekly Report (2007;56 [RR-6]:1-40).

New recommendations for the upcoming flu season include the following:

► **For health care administrators.** Treat the vaccination of health care personnel as a patient safety issue and implement ways to encourage all health care providers to get flu shots. For example, require signed statements from health care providers who decline flu vaccination.

► **For clinicians.** In addition to those who were not previously vaccinated, those children aged 6 months to 8 years who received only one dose of flu vaccine in earlier years should receive two doses this year. Administer a second dose of the trivalent inactivated influenza vaccine (TIV) at least 4 weeks after the first dose. Clinicians who are using the live, attenuated influenza vaccine (LAIV) for these children should give a second dose at least 6-10 weeks after the first dose.

The TIV may be used for any person aged 6 months and older, including those with high-risk conditions. The LAIV is currently approved only for healthy, nonpregnant individuals aged 5-49 years. The influenza vaccine for the 2007-2008 season contains a new strain called A/Solomon Islands/3/2006 (H1N1)-like, along with two strains that have been used in previous vaccines: A/Wisconsin/67/2005 (H3N2)-like and B/Malaysia/2506/2004-like viruses.

Vaccination coverage continues to fall short of the CDC's recommendations, and the CDC encourages clinicians to be proactive about vaccinating their patients and to offer vaccination throughout the flu season.

As in recent years, the CDC recommends annual vaccination for the following groups:

► Anyone (including school-aged children) who wants to reduce the risk of getting or transmitting the flu.
► All children aged 6 months to 4 years.
► All adults aged 50 years and older.
► Children and teens aged 6 months to 18 years who receive long-term aspirin therapy.
► Pregnant women or women who plan to be pregnant during the flu season.
► All persons with chronic pulmonary, cardiovascular, liver, kidney, or metabolic disorders, including diabetes but excluding hypertension.
► All persons with conditions that could impede respiratory function (such as cognitive dysfunction, spinal cord injuries, or other neuromuscular problems).
► All immunosuppressed persons.
► Health care personnel.
► Healthy household contacts and caregivers of children younger than 5 years or of adults aged 50 years and older.
► Healthy household contacts and caregivers of anyone with a medical condition that increases the risk for influenza complications.
► Individuals in nursing homes or chronic care facilities.

Updates to the 2007-2008 flu vaccination recommendations will be posted on the CDC's Web site at www.cdc.gov/flu. ■

Flu Vaccines Have Comparable Immunogenicity and Safety

BY MIRIAM E. TUCKER
Senior Writer

BALTIMORE — GlaxoSmithKline's influenza vaccine, Fluarix, is noninferior to Sanofi Pasteur's Fluzone in adults aged 18-95 years, Dr. James D. Campbell reported at a conference on vaccine research sponsored by the National Foundation for Infectious Diseases.

The two vaccines were comparable in terms of immunogenicity, tolerability, and safety in a postmarketing study conducted by GSK at the request of the U.S. Food and Drug Administration following the licensure of Fluarix in 2005.

Immunogenicity of both vaccines was lower in adults aged 65 years and older, however, suggesting the need for improved formulations for this population, said Dr. Campbell of the center for vaccine development at the University of Maryland, Baltimore.

The 1,820 adults randomized to either Fluarix or Fluzone had a median age of 68 years, 92% were white, and 59% were women. Approximately two-thirds of each vaccine group were aged 65 years and older. A total of 1,739 subjects—872 of whom received Fluarix and 867 of whom received Fluzone—completed the study protocol.

Local reactions with both vaccines were nearly all mild or moderate, most lasting just a few days. Severe (grade 3) reactions occurred in 0.2% of the group taking Fluarix and 1.4% of those taking Fluzone. Headache and fatigue were the most common general reactions, occurring in 12%-13% with each vaccine. Severe general reactions were equally rare in both groups, at 1.2% with Fluarix and 1.6% with Fluzone. No category of unsolicited adverse events was markedly more common after either vaccine. Serious adverse events occurred in 5% of participants in each group; none of the adverse events were deemed related to the vaccine, Dr. Campbell said.

Immunologic noninferiority was the primary end point, defined by a geometric mean antibody titer (GMT) response to Fluarix not less than two-thirds that of Fluzone, and a less than 10% difference in seroconversion at day 21 between the two vaccines. Fluarix was immunologically noninferior to Fluzone for all three vaccine strains in the study population as a whole and in the elderly subset.

However, both seroconversion and GMT responses to the H1N1 strain were slightly better with Fluarix; Fluzone produced a slightly higher GMT response to the B strain than did Fluarix, but seroconversion rates were similar.

Both types of responses were diminished in the elderly subjects, compared with the entire group, but did not differ by vaccine. Seroprotection is estimated at 82%-98% for both vaccines, Dr. Campbell said. ■