



DEPARTMENT OF VETERANS AFFAIRS
Veterans Health Administration
Washington DC 20420

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In Reply Refer To: 11

September 21, 2007

UNDER SECRETARY FOR HEALTH'S INFORMATION LETTER
VACCINATION TO PREVENT HERPES ZOSTER

1. Purpose: This Under Secretary for Health Information Letter provides information about the provision of a vaccine to prevent herpes zoster within the Veterans Health Administration (VHA) facilities.

2. Background

a. Herpes zoster (HZ), also known as "shingles," is a condition with significant morbidity and effect on health-related quality of life in the older adult population. HZ results from reactivation of latent varicella zoster (VZ) virus within the spinal dorsal root ganglia. Over 90 percent of adults in the United States (US) have serologic evidence of varicella (chicken pox) infection and are at risk for HZ. Persons at highest risk for HZ include immunocompromised individuals and the elderly. The annual incidence of HZ is approximately 1.5 - 4.0 cases per 1,000 people and is estimated to be as high as 10 cases per 1,000 persons among those age over 75 years. The lifetime risk of HZ is estimated at 10 - 20 percent. The most common complication of HZ is postherpetic neuralgia (PHN), defined as the persistence of sensory symptoms (pain, numbness, or dyesthesias) in the affected dermatome for more than 30 days after the onset of zoster. PHN occurs with a reported incidence of 10 - 33 percent. As with HZ, the risk increases with advancing age.

b. In May 2006, the U.S. Food and Drug Administration licensed the first vaccine (Zostavax[®], Merck & Co., Inc.) for the prevention of HZ for use in adults age 60 and over.

(1) The major scientific study which evaluated the clinical effectiveness of Zostavax[®] is the "Shingles Prevention Study," a Department of Veterans Affairs (VA) Cooperative Studies Program study. This randomized, placebo-controlled, double-blind clinical trial was conducted in 38,546 adults age 60 and older. Median follow-up time was 3.1 years.

(2) The burden of illness score, a composite measure incorporating both severity of pain and discomfort and duration of illness, was reduced by 61.1 percent (95 percent Confidence Interval (CI) 51.1, 69.1) for the vaccinated group, compared to the placebo group. The incidence of HZ in the vaccinated group was reduced by 51.3 percent (95 percent CI 44.2, 57.6; 5.4 per 1000 person-years versus 11.1 in the placebo group). Age showed an apparent inverse relationship with vaccine efficacy; the efficacy of the vaccine in persons age 80 and older is uncertain. The number of people needed to vaccinate to prevent one additional case of shingles over a 3-year period is 59 (95 percent CI 37, 143).

c. The numbers of hospitalizations and deaths were similar between the vaccinated and placebo groups. A statistically significant increase in the rate of serious adverse events was seen in the vaccinated group relative to the placebo group in an adverse event monitoring substudy; however, no body system, clinical syndrome, or diagnosis was responsible for the group difference and no temporal clustering of serious adverse events was seen relative to the zoster vaccine. A difference between groups in serious adverse events was not observed in the routine safety monitoring cohort. The most common adverse event overall was a local injection site reaction including redness, swelling, rash, and pain; this was more common in the vaccinated group compared to placebo (48 percent versus 16 percent).

d. Because it is so new, few economic analyses of Zostavax[®] have been done; thus the cost-effectiveness of the vaccine is uncertain.

e. In Fiscal Year (FY) 2005, there were 4.1 million enrolled veterans who were ages 60 and older. Of these, 2.9 million VA enrollees had a visit, at least once, in the previous 2 years and did not have any of the contraindicated conditions that would prevent them from being eligible for the vaccine. The lowest current per-dose cost of the vaccine for VA is \$113 (pricing that is subject to change).

3. Recommendations of Center for Disease Control and Prevention's (CDCs) Advisory Committee on Immunization Practices (ACIP). In October 2006, the ACIP issued provisional recommendations for Zostavax[®]. These recommendations will become final when published in the CDC's Morbidity and Mortality Weekly Report. The provisional recommendation is as follows: *"A single dose of zoster vaccine is recommended for adults 60 years of age and older whether or not they report a prior episode of herpes zoster. Persons with chronic medical conditions may be vaccinated, unless a contradiction or precaution exists for their condition."*

4. Considerations for Use within VHA Facilities

a. The zoster vaccine is available for use within VHA facilities. Providers may consider vaccinating adults 60 years of age and older with a single dose of zoster vaccine, unless a contraindication or precaution exists. A single dose of 0.65 ml is administered subcutaneously in the outer aspect of the upper arm.

b. The vaccine is contraindicated in the following persons:

(1) Those with a history of anaphylactic reaction to gelatin, neomycin, or any other component of the vaccine.

(2) Those with primary or acquired immunodeficiency states, including leukemia; lymphomas of any type, or other malignant neoplasm affecting the bone marrow or lymphatic system; or AIDS or other clinical manifestations of infection with HIV.

(3) Those with active, untreated tuberculosis.

- (4) Those on immunosuppressive therapy, including high-dose corticosteroids.
- (5) Those receiving cancer chemotherapy or radiation therapy.
- (6) Women who are or may be pregnant.

c. Common adverse effects of the vaccine are injection-site reactions (erythema, pain, and/or tenderness, rash, and swelling), which are generally mild and resolve in a few days.

d. Persons with a minor illness, such as a cold, may be vaccinated. But persons who are moderately or severely ill, including having a fever of 101.3° (38.5°) or higher, usually need to wait until they recover before being vaccinated.

e. All persons receiving the vaccine must be given the current Vaccine Information Statement, available from the CDC Web site at: <http://www.cdc.gov/nip/publications/VIS/vis-shingles.pdf>.

f. Transmission of the vaccine virus may rarely occur between vaccinees who develop a varicella-like rash and susceptible contacts. Transmission of the vaccine virus from vaccinees without a varicella-like rash has been reported, but not confirmed. Weigh the risk of transmission of the attenuated virus to a susceptible contact against the risk of developing natural zoster that could be transmitted to a susceptible individual.

g. The duration of protection after a vaccination with the herpes zoster vaccine is not known. The Shingles Prevention Study demonstrated protection through 4 years of follow-up. The need for revaccination has not been defined.

h. Details about vaccine characteristics and handling are in Attachment A. More detailed information is on the Pharmacy Benefits Management Web site at: http://www.pbm.va.gov/monograph/Zoster_percent20Vaccine_percent20Monograph.pdf.

i. The CPT code for Zostavax[®] is 90736 (Zoster shingles vaccine live for subcutaneous administration). The International Classification of Diseases 9th edition (ICD-9) code that can be used for patients receiving vaccination is V04.89 (need for prophylactic vaccination and inoculation against certain viral diseases—other).

j. Providers are encouraged to work with clinical pharmacists to report all clinically-significant adverse events, even if a causal relationship to the vaccine is not certain.

- (1) Web-based reporting is available at <https://secure.vaers.org/VaersDataEntryintro.htm>.
- (2) Reports can also be made by telephone (800-822-7967).

k. Providers are strongly encouraged to enter allergies and/or adverse reactions into the allergies and/or adverse reactions data field in the Computerized Patient Record System (CPRS), to allow others to see that the patient has had a reaction. **NOTE:** A link to “How to Enter an

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Allergies and Adverse Reactions for CPRS v.26 is on the Center for Medication Safety Web site at: <http://vawww.pbm.va.gov/pbm/vamedsafe.htm>.

1. Facilities are encouraged to develop and implement vaccination protocols. Local clinical reminders may be developed, but their use is not required.

5. References and Resources

a. Advisory Committee on Immunization Practices. "Provisional Recommendations for the Use of Zoster Vaccine," at: http://www.cdc.gov/nip/recs/provisional_rec/zoster-11-20-06.pdf

b. Albrecht MA. Treatment and Prevention of Herpes Zoster," Up To Date, Rose BD (Ed), Waltham, MA, 2007.

c. Crove D, Bajwa ZH, Warfield CA. Postherpetic neuralgia. In: Up To Date, Rose BD (Ed), Waltham, MA, 2007.

d. Gnann JW Jr, Whitley RJ. "Clinical Practice. Herpes Zoster," New England Journal of Medicine (N Engl J Med). 2002;347:340-6.

e. Kimberlin DW, Whitley RJ. "Varicella-zoster Vaccine for the Prevention of Herpes Zoster," N Engl J Med. 356:1338-43; 2007.

e. Merck & Co., Inc. Zostavax [Zoster Vaccine Live (Oka/Merck)] Package Insert. Whitehouse Station, NJ. Issued May 2006, at: http://www.merck.com/product/usa/pi_circulars/z/zostavax/zostavax_pi.pdf

f. Oxman MN, Levin MJ, Johnson GR, Schmader KE, Straus SE, Gelb LD et al for the Shingles Prevention Study Group. "A Vaccine to Prevent Herpes Zoster and Postherpetic Neuralgia in Older Adults," N Engl J Med. 352:2271-84: 2005

6. Inquiries. Questions regarding this information letter are directed to the Director, VA National Center for Health Promotion and Disease Prevention (NCP) at (919) 383-7874, ext 222; Chief Consultant, Pharmacy Benefits Management (119) at (202) 273-5086; or Chief Public Health and Environmental Hazards Officer (13) at (202) 273-8575.

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ATTACHMENT A

VACCINE CHARACTERISTICS AND HANDLING

1. The Zostavax[®] vaccine mechanism of action is to boost VZ virus cell-mediated immunity, thereby protecting against Herpes zoster (HZ) and its complications. While both the varicella vaccine (Varivax[®]) and Zostavax[®] contain the same live-attenuated varicella virus, the varicella vaccine is not a substitute for Zostavax[®] as it contains a substantially lower dose of virus that may not result in an appropriate immune response. Zostavax[®] vaccine is supplied in single dose vials as a preservative-free powder that requires reconstitution prior to administration. A single dose of 0.65 milliliter (ml) is administered subcutaneously in the outer aspect of the upper arm.
2. The Zostavax[®] vaccine component should be stored frozen at an average temperature of -15° Centigrade (C) (+5° Fahrenheit (F)) or colder until reconstituted for injection. Any stand-alone freezer or separately-closing freezer compartment of a refrigerator that reliably maintains this average temperature is sufficient for storage. The supplied diluent needs to be stored separately at room temperature (20°-25° C, 68°-77° F) or in the refrigerator (2°-8° C, 36°-46° F). The vaccine needs to be administered immediately after reconstitution and discarded if not used within 30 minutes. It is never to be refrozen.