Herpes Zoster Vaccination
Eliesha Daniels, PharmD

Introduction
Herpes zoster, commonly known as shingles, is a viral infection that is caused by the varicella-zoster virus (VZV).\textsuperscript{1} Over 90% of adults in United States have serologic evidence of VZV infection and are at risk for herpes zoster.\textsuperscript{1} The incidence of herpes zoster ranges from 2.2–3.4 cases/1000 person-years, with as many as half a million new cases occurring annually.\textsuperscript{2} The lifetime risk of herpes zoster is estimated to be 10-20%.\textsuperscript{3} Risk and severity of illness increase with advancing age, with peak prevalence occurring after 50 years of age. The incidence of herpes zoster among individuals older than 75 years of age exceeds 14 cases/1000 person-years.\textsuperscript{2}

Background
VZV is an exclusively human pathogen, that usually infects people during childhood and causes varicella, commonly known as chickenpox.\textsuperscript{4} After causing vesicular lesions of the skin, the virus enters the dorsal root ganglia and lays dormant.\textsuperscript{4,5,6} The virus remains latent throughout the majority of life due to acquired cell-mediated immunity. However, as a person ages, this immunity weakens, and the virus can be reactivated to cause a secondary infection, known as herpes zoster.\textsuperscript{5,6} Stress, trauma, immunosuppression, and surgery can reactivate VZV and increase the risk for herpes zoster.\textsuperscript{4,5} Herpes zoster infection has also been reported in younger patients but to a much lesser extent.\textsuperscript{5}

Herpes zoster usually begins with a prodromal phase, in which patients report headache, photophobia, and malaise, but rarely fever. Any time from two days to up to three weeks after the prodromal phase, the characteristic skin lesions occur. These lesions first appear as a unilateral macropapular rash that follow a distinct belt-like pattern and later erupt to form vesicles. Within ten days, the lesions erupt and crust over, usually healing within two to four weeks without treatment. However, prompt treatment can speed the healing process and decrease pain and the risk of complications.\textsuperscript{1,2,5}

Complications associated with herpes zoster include bacterial superinfection, scarring, allodynia, motor paralysis, meningoencephalitis, transverse myelitis, cerebral vasculitis, pneumonitis, visual impairment, hearing loss, myocarditis, pancreatitis, esophagitis, and postherpetic neuralgia. The most common complication of herpes zoster is postherpetic neuralgia, occurring in 10-18% of patients. Symptoms of postherpetic neuralgia include stabbing, burning, aching, and electric-shock-like pain persisting more than 30 days after lesions have healed.\textsuperscript{4,5,6}

Treatment options for the complications associated with herpes zoster have been primarily targeted at disease state management and symptom relief.\textsuperscript{6} In May 2006, the U.S. Food and Drug Administration (FDA) approved a live attenuated zoster vaccine for the prevention of herpes zoster in adults age 60 years and older. In October 2006, the Centers for Disease Control and Prevention’s Advisory Committee on Immunization Practices (ACIP) recommended that all patients age 60 years and older should be offered the vaccine as part of standard immunization.\textsuperscript{2,4,5} In March 2011, the FDA approved an expanded age indication for the live attenuated zoster vaccine in adults 50 years of age and older.\textsuperscript{7}
**Zostavax® (zoster vaccine live)**

It has been proposed that immunity to VZV plays an important role in the pathogenesis of herpes zoster and cell-mediated immunity to VZV is a major determinant of the risk and severity of herpes zoster. Therefore, the immunization of older adults with a VZV vaccine, like Zostavax®, will boost their cell-mediated immunity to VZV and reduce the risk of herpes zoster and postherpetic neuralgia.\(^8,9\)

Zostavax®, a lyophilized preparation of the Oka/Merck strain of live, attenuated VZV. The virus was initially obtained from a child with naturally-occurring varicella and then introduced into human embryonic lung cell cultures. It was adapted to and propagated in embryonic guinea pig cell cultures and finally propagated in human diploid cell cultures. Each 0.65 ml dose contains a minimum of 19,400 plaque-forming units (PFU) of the of the Oka/Merck strain of VZV, which is at least 14 times the potency of the varicella vaccine (Varivax®).\(^2,4\)

Zostavax® is indicated for prevention of herpes zoster (shingles) in individuals 50 years of age and older and is not indicated for the treatment of zoster or postherpetic neuralgia or as a substitute for live varicella virus vaccine. It is not indicated for use in children or persons less than 50 years of age as there is insufficient data to recommend vaccination in these groups at this time.\(^2,4,8\) Even though the safety and efficacy of Zostavax® have not been studied in patients with a history of herpes zoster infection, these persons can still be vaccinated without any additional safety concerns.\(^4,5\)

Efficacy of Zostavax® was originally evaluated in the Shingles Prevention Study,\(^8\) a placebo-controlled, double-blind clinical trial in which 38,546 subjects 60 years of age or older were randomized to receive a single dose of either Zostavax® or placebo. Subjects were followed for the development of herpes zoster for a median of 3.1 years. The primary efficacy analysis included all subjects randomized in the study who were followed for at least 30 days post-vaccination and did not develop a case of herpes zoster within the first 30 days post-vaccination. Zostavax® significantly reduced the incidence of herpes zoster by 51.3% and postherpetic neuralgia by 66.5%.\(^8\) Vaccine efficacy for the prevention of herpes zoster was highest for those subjects 60–69 years of age and declined with increasing age. Overall risk for postherpetic neuralgia was significantly decreased by 39% for those who developed herpes zoster despite vaccination.\(^4\) However, the vaccine's efficacy against postherpetic neuralgia achieved statistical significance relative to placebo only among persons 70–79 years of age. The vaccine was substantially less effective in preventing postherpetic neuralgia occurrence in individuals age 60–69 years or 80 years and older. Vaccination was also linked to a small decrease in the overall duration of postherpetic neuralgia (20 vs. 22 days).\(^8\)

Efficacy of Zostavax® was reevaluated in the Zostavax® Efficacy and Safety Trial (ZEST), a placebo-controlled, double-blind, clinical trial in which 22,396 subjects 50–59 years of age were randomized to receive a single dose of either Zostavax® or placebo.\(^7\) Study subjects were monitored for the development of shingles for a median of 1.3 years (range zero to two years) after receiving vaccination. Participants also were followed for adverse events for 42 days post-vaccination and for serious adverse events through six months post-vaccination. Thirty cases of shingles occurred in the vaccine group versus ninety-nine cases of shingles in the placebo group and efficacy of the vaccine was 69.8 percent. There was an overall higher incidence of adverse events in the vaccine group versus the placebo group and this difference was primarily due to different rates of injection-site adverse events (63.6 percent for vaccine vs. 14.0 percent for placebo). The overall incidence of systemic adverse events reported within 42 days of vaccination was higher for Zostavax® than for placebo (35.4 percent for vaccine vs. 33.5 percent for placebo); however, no significant differences were observed between the two study groups for any individual systemic adverse event with the exception of pain in the extremity and headache. Serious adverse events occurred at a similar rate in subjects vaccinated with Zostavax® or placebo within 42 days of vaccination (0.6 percent for vaccine vs. 0.5 percent for placebo) and 182 days of vaccination (2.1 percent for vaccine vs. 1.9 percent for placebo). An anaphylactic reaction was reported for one study participant who received Zostavax®.\(^7\)
Zostavax® should not be used in persons receiving immunosuppressive therapy, including high-dose corticosteroids (≥20 mg/day of prednisone or equivalent) lasting two or more weeks and in women who are or may become pregnant. Use of the live attenuated vaccine in immunosuppressed individuals may result in a more extensive vaccine-associated rash or disseminated disease. In addition, this vaccine is contraindicated in persons with a history of anaphylactic reaction to gelatin, neomycin, or any other component of the vaccine; those with a history of primary or acquired immunodeficiency states, including leukemia, lymphomas of any type, or other malignant neoplasms affecting the bone marrow or lymphatic system; patients with AIDS or other clinical manifestations of infection with human immunodeficiency viruses; and those with active untreated tuberculosis.

Zostavax® and Pneumovax® 23 should not be given concurrently because concomitant use resulted in reduced immunogenicity of Zostavax®. Coadministration of the herpes zoster virus vaccine and the trivalent inactivated influenza vaccine led to a similar antibody response to both vaccines four weeks after vaccination as compared with the antibody response when the herpes zoster virus vaccine was given four weeks after the trivalent inactivated influenza vaccine. Therefore, with the exception of Pneumovax® 23, the herpes zoster virus vaccine may be administered concurrently with inactivated or live vaccines, but each vaccine must be administered using a separate syringe at a different anatomic site. The herpes zoster virus vaccine can be administered at any time before or after an inactivated vaccine. In contrast, if not simultaneously administered, the herpes zoster virus vaccine needs to be administered at least four weeks before or after another live, attenuated vaccine. Concurrent administration of the herpes zoster virus vaccine and antiviral medications has not been evaluated.

The most common side effects reported with the use of Zostavax® were injection-site adverse events (redness, pain, warmth, tenderness, swelling, and itching) and headache, 48.3% and 6.3%, respectively. There were no serious adverse events observed with any different frequency between persons who received the vaccine versus placebo.

Zostavax® is supplied as single-dose vials of lyophilized vaccine and single-dose vials of diluent. A volume of 0.65 ml of zoster vaccine live is administered subcutaneously, preferably in the upper arm. Administration should occur immediately after reconstitution to reduce loss of potency. If not administered within 30 minutes of reconstitution, zoster vaccine live should be discarded.

Zostavax® is not covered under the Medicare Part B program; however, since it is a preventive vaccine, it is available for reimbursement under the Medicare Part D program.

**Conclusion**

Herpes zoster, or shingles, is a very prevalent disease affecting older adults. The complications associated with herpes zoster can be very debilitating and have a severe impact on a person’s quality of life, both physically and emotionally. Until recently, treatment options have been primarily targeted at disease state management and symptom relief. Zostavax® is the first vaccine approved for the prevention of herpes zoster in adults age 50 years and older. The vaccine has been proven to be effective in preventing herpes zoster infection and decreasing the incidence of complications associated with the disease including postherpetic neuralgia.

**Additional Resources**

http://www.niaid.nih.gov/topics/shingles/Pages/Default.aspx  
http://www.cms.gov/PrescriptionDrugCovGenInp/
References

To report medical fraud, contact the Medicaid Quality Assurance Bureau at [NM Medicaid Fraud@state.nm.us](mailto:NMMedicaidFraud@state.nm.us) or (505) 827-3100. We appreciate your continued support of our efforts to encourage quality care for our Medicaid clients.

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