Policy Statement

Recommendations for Herpes Zoster Vaccine for Patients 50 Years of Age and Older

Herpes zoster is a serious health problem in the United States. Current estimates of new cases in the United States are up to 1.2 million annually, approximately 20% of which are herpes zoster ophthalmicus (HZO).1 It is estimated that 1 in 3 people will have herpes zoster in their lifetime. Although it is more common and severe in immunocompromised persons, the vast majority (>90%) of patients with herpes zoster are not immunocompromised. Although the incidence of herpes zoster goes up significantly with age, starting at 40 years, the number of cases is highest in people 50 to 59 years of age.2-4 In one Centers for Disease Control and Prevention (CDC) study, the mean age of onset was 52 years.5 Risk factors for the development of herpes zoster include increased age, immunocompromised status, female gender, severe physical limitation,6 heart failure,7 traumatic brain injury,8 diabetes,1 acute kidney failure,2 and depression.9

Disease Complications and Costs

The complications and sequelae of herpes zoster can be severe and long term, even—rarely—resulting in death.11 The medical costs incurred by herpes zoster and its complications, including direct costs from acute and chronic pain, eye complications, secondary infections, and neuropathies, are estimated to be $1 billion,12 with indirect costs from lost work and work productivity adding to that total, especially in younger age groups such as those 50 to 59 years of age.13

Ocular complications of herpes zoster include infectious and inflammatory anterior and posterior segment disease, neurotrophic ocular surface disease, and eyelid malposition and scar. Severe, irreversible vision loss may result from corneal opacification, glaucoma, and retinal disease.14 Approximately 20% of individuals affected by HZO experience potentially serious ocular disease, such as keratitis, uveitis, glaucoma, or neurotrophic disease. The 10-year probability of severe visual loss (20/200 or worse), a serious eyelid malposition, or chronic trichiasis developing varies between 2% and 9% depending on the treatment of the disease. Early recommended treatment with systemic antiviral therapy may decrease the incidence or severity of serious sequelae, but the likelihood of preventing complications is reduced if therapy is delayed, usually considered to be after more than 3 days of initial symptoms15 or rash. Postherpetic neuralgia is more likely in older patients, in patients with more severe acute pain and rash, and in patients with ophthalmic involvement.16,17

Systemic complications of herpes zoster include stroke, which is more common after HZO than herpes zoster in other locations,18-21 temporal arteritis,22 and possibly heart attack23,24 and depression.25

Evaluation of Current Evidence

Recent evidence seems to indicate that the age of onset of herpes zoster is decreasing, and this effect may be unrelated to herpes zoster vaccination. Two studies reported a significant 5-year decrease in the mean age of onset of herpes zoster from older than 60 years to younger than 60 years.26,27 Both studies recommended that vaccination age may need to be lowered to 50 years. The mean age of patients experiencing HZO-related ocular disease is 63 years in another publication.28

Effectiveness of Vaccinations and Recommendations of Other Organizations

Zoster Vaccine Live (Zostavax)

A randomized, controlled clinical trial demonstrated that zoster vaccine live (ZVL; an attenuated live virus vaccine; Zostavax; Merck & Co, Inc, Whitehouse Station, NJ) decreased the incidence of herpes zoster by 51% and the occurrence of postherpetic neuralgia by 66% in immunocompetent people 60 years of age and older.29 The vaccine decreased the incidence of herpes zoster by more than 60% in people 60 to 69 years of age compared with less than 40% in people 70 years of age and older. However, the effect on disease severity was greater in older persons, resulting in similar reduction in disease burden across age groups. An important limitation of ZVL is its waning effect, and models estimate nearly complete loss of efficacy by 10 years after vaccination.

On the basis of this study, ZVL was approved by the United States Food and Drug Administration (FDA) in 2006 and recommended by the CDC in 2008 for immunocompetent people 60 years of age and older. The CDC also recommended herpes zoster vaccine for people with chronic medical conditions, including those affecting humoral immunity, and people who anticipate becoming immunocompromised. In the United States, the low rate of herpes zoster vaccination is a public health problem. According to 2015 CDC data, only 31% of eligible people 60 years of age and older had received a herpes zoster vaccine.30
In 2011, the FDA expanded their approval of the vaccine to include immunocompetent people 50 to 59 years of age, after it was shown to decrease the incidence of herpes zoster by 70% in this age group. The CDC recommendation for ZVL remains unchanged.

Recombinant Zoster Vaccine (Shingrix)
The recombinant zoster vaccine (RZV; Shingrix, Glaxo-SmithKline, Philadelphia, PA) also called the herpes zoster subunit vaccine, contains a recombinant varicella zoster virus glycoprotein E surface antigen reconstituted in a novel liposome-based adjuvant system. A clinical trial (Zoster Efficacy Study in Adults 50 Years of Age or Older [ZOE-50]) of the RZV compared with placebo conducted outside of the United States from 2010 through 2011, the results of which were published in 2015, demonstrated that this vaccine had an efficacy of approximately 97% in all age groups. The results of the second part of this trial (Zoster Efficacy Study in Adults 70 Years of Age or Older [ZOE-70]), which was conducted concurrently and included participants 70 years of age and older, were pooled with ZOE-50 and showed an approximately 90% efficacy in vaccine recipients 70 years of age and older. The efficacy of this vaccine remained 85% against herpes zoster after 4 years. Local or acute systemic reactions, or both, interfering with normal activities occurred in more than 10% of vaccine recipients, raising concern about adherence to the 2-dose schedule required for efficacy. In vitro studies report that the immune response is not inferior in people with a past history of vaccination with ZVL or herpes zoster or when given at the same time as influenza vaccine.

Food and Drug Administration Approval
The RZV was approved by the FDA in October 2017 for adults 50 years of age and older. This vaccine is administered intramuscularly as a 2-dose series 2 to 6 months apart. It is refrigerated and must be discarded if frozen before or after reconstitution. According to the FDA label, acute local and general reactions occur more often in people 50 to 69 years of age than in those older than 70 years, and general or systemic reactions occur more frequently after the second dose than the first dose of the 2-dose series.

Centers for Disease Control and Prevention Recommendations
In January 2018, the Advisory Committee on Immunization Practices of the CDC recommended the RZV vaccination of immunocompetent adults 50 years of age and older, including people with a history of vaccination with ZVL at least 2 months previously. The CDC states that it is important to counsel patients regarding the possibility of acute local and systemic reactions and to encourage patients to complete the 2-dose series. With regard to the timing of vaccination with the 2-dose series of the RZV in people with a past history of vaccination with ZVL, the CDC notes one should consider the age at and time of vaccination with ZVL, which was less effective in preventing herpes zoster in people 70 years of age and older than in people 60 to 69 years of age, when vaccination with the RZV was studied 5 years after vaccination with ZVL. The CDC recommends the RZV as the preferred vaccine over ZVL because of its higher and longer-lasting efficacy across all age groups. The CDC issued no recommendations for immunocompromised persons because they were excluded from the clinical trials. According to the CDC, reporting of adverse events, using the Vaccine Adverse Events Reporting System (phone, 1-800-822-7967) and Vaccine Safety Datalink, is especially important because of the novel adjuvant that the RZV contains with high reactivity and immunogenicity.

Additional Considerations
People with a history of HZO may be at risk for recurrent eye disease after vaccination with the RZV, as has been reported in some cases after vaccination with ZVL. It is suggested that patients with a history of HZO should be examined by their ophthalmologist within several weeks before and after vaccination against herpes zoster, and adverse events should be reported. The optimal timing of vaccination after an episode of herpes zoster, including HZO, is not specified by the CDC. An episode of herpes zoster stimulates cell-mediated immunity for a period of time, so vaccination is not urgent. It is suggested that vaccination should be delayed after HZO until eye disease is well controlled.

Comparisons between Recombinant Zoster Vaccine and Zoster Vaccine Live
The CDC recommends the RZV as the preferred vaccine over ZVL, although there are no head-to-head studies comparing the 2 vaccines. In our opinion, if compliance with the second injection of the RZV required for efficacy is doubtful, and concern about acute local and general reactions is a barrier to RZV vaccination, ZVL is an option to consider, especially in immunocompetent adults 50 to 59 years of age, among whom ZVL reduces herpes zoster by 70% and has fewer systemic reactions.

Conclusions
Both the RZV and ZVL are FDA approved for individuals 50 years of age and older, but as of 2018, the CDC now recommends vaccination against herpes zoster with the RZV for immunocompetent adults 50 years of age and older. Vaccination starting at 50 years of age will reduce the burden of this disease, including chronic eye disease. Ophthalmologists should recommend strongly that patients 50 years of age and older without contraindications obtain vaccination with the RZV and should work with primary care physicians, internists, dermatologists, other medical doctors, and health care professionals to recommend vaccination strongly against herpes zoster starting at 50 years of age. Given the currently low rate of ZVL immunization in indicated age groups, advocacy by ophthalmologists may play an important role in increasing vaccination rates in the future.


Footnotes and Financial Disclosures

Originally received: June 30, 2018.
Final revision: June 30, 2018.
Accepted: July 5, 2018.
Financial Disclosure(s):
The authors have no proprietary or commercial interests in any materials discussed in this article.

Approved by: Cornea Society Executive Committee, April 2018 and the American Academy of Ophthalmology Board of Trustees, June 2018.

HUMAN SUBJECTS: Human subjects were not included in this study.
No animal subjects were included in this study.

Abbreviations and Acronyms:
CDC = Centers for Disease Control and Prevention; FDA = United States Food and Drug Administration; HZO = herpes zoster ophthalmicus; RZV = recombinant zoster vaccine; ZVL = zoster vaccine live.

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