Herpes zoster (ie, shingles) will develop in approximately 1 in 3 persons during their lifetimes, resulting in an estimated 1 million episodes of herpes zoster in the United States annually.¹ Complications from herpes zoster, including chronic pain, scarring, loss of vision, and hospitalization (and any combination of these), occur in as much as 25% of cases.¹ One’s risk for herpes zoster increases with age, as do the risks of complications that occur during and after the syndrome.¹ As summarized in the article by Hendriksz et al² in the present supplement to JAOA—The Journal of the American Osteopathic Association, the primary varicella-zoster virus infection (ie, chickenpox) typically occurs in childhood or young adulthood. After the virus lies dormant for several years, it becomes reactivated in a dorsal root ganglion, leading to the symptoms of herpes zoster (eg, fever, headache, malaise, itching, severe pain down the nerve root, vesicular skin rash along the same dermatome) and subsequent sequelae and complications—primarily a neuropathic pain syndrome called postherpetic neuralgia (PHN).³⁵

In May 2006, the US Food and Drug Administration (FDA) licensed Zostavax (Merck & Co Inc, Whitehouse Station, NJ), a live attenuated vaccine for prevention of herpes zoster and its sequelae in adults aged 60 years or older.⁶ This vaccine is not presently indicated for individuals who have received the varicella vaccine (Varivax; Merck & Co Inc) or children. In October 2006, the Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention recommended that Zostavax be routinely offered to adults aged 60 years or older—excepting immunocompromised persons or persons with known hypersensitivities—regardless of whether a history of shingles is evident (Figure).⁷

**Update on FDA-Approved Uses and ACIP Recommendations**

In 2010, researchers at Merck & Co, Inc completed the Zostavax Efficacy & Safety Trial (ZEST), focusing on the use of herpes zoster vaccine in individuals aged between 50 and 59 years.⁸⁹ In March 2011, after reviewing data from ZEST, the FDA extended indications for the herpes zoster vaccine to include adults aged 50 to 59 years.⁹ In June 2011, however, the ACIP declined to make a recommendation that this vaccine be routinely offered to persons in the 50- to 59-year age group. The ACIP cited several reasons for its decision, none of which were related to the efficacy or safety of the vaccine.¹⁰ The advisory committee’s decision was based on various practical considerations, as summarized in the following text.

The ACIP noted that a national health survey in 2009 suggested that 90% of Americans aged 60 years or older remained unvaccinated against herpes zoster, despite the availability of a safe, effective, FDA-approved vaccine since 2006.¹⁰ The advisory committee also expressed concerns about limited supplies of herpes zoster vaccine, resulting from increases in demand coincident with the flu season.
with increased publicity and diversion of manufacturing priorities to the varicella vaccine.\textsuperscript{10} If the limited supplies are further diverted toward vaccination of people younger than 60 years before individuals in the older, higher-risk age group are vaccinated, physicians would have to explain the lack of available vaccine to their older patients. Such a development could further decrease the likelihood of this older population getting vaccinated.

The Merck & Co, Inc, trials showed that the efficacy of herpes zoster vaccine is age dependent, with greater efficacy seen in younger age groups (50-59 years, 70\% efficacy) compared to older age groups (\textgeq\,80 years, 20\% efficacy).\textsuperscript{11} When all age groups were analyzed together, the overall efficacy of herpes zoster vaccine was about 50\%.\textsuperscript{11}

In an analysis by Kaiser Permanente Southern California, a cohort of more than 75,000 patients aged 60 years or older who received herpes zoster vaccine after it became available on the market was compared to age-matched unvaccinated control subjects.\textsuperscript{12} In that comparison, the efficacy of the vaccine remained fairly constant among all age strata within the studied age group.\textsuperscript{12}

Some of the differences in vaccine efficacy seen across different studies and different cohorts may relate to varying follow-up times and trial designs. Nonetheless, herpes zoster vaccine shows efficacy across all age groups 50 years or older.\textsuperscript{6,9} However, the long-term duration of immunity from this vaccine is not known, and older individuals may require a booster 20 to 30 years after the initial vaccination (if they received the vaccination when aged in their 50s). Even if the vaccine reduces a patient’s risk of herpes zoster by half for 2 additional decades, this result may be important, because the likelihood of acquiring the condition increases as one ages beyond 50 years. Likewise, if a vaccinee were to acquire herpes zoster but with fewer complications and long-term sequelae than would be the case without vaccination, this result would be important to at-risk groups.

Zostavax remains indicated only for herpes zoster prevention and not for treatment.\textsuperscript{9} This vaccine should be offered to the patient regardless of whether the patient recalls a history of having had shingles. The safety review for this vaccine suggests a high degree of safety, with the majority of adverse events pertaining to localized injection site reactions with pain and swelling.\textsuperscript{7,9,13} A contraindication to this vaccine is a history of anaphylactic reaction (as opposed to localized contact dermatitis, which is not a contraindication) to any component of the vaccine, including gelatin or neomycin sulfate (Figure).\textsuperscript{6,9}

**Clinical Application**

It is important to remember that although the ACIP does not currently recommend the herpes zoster vaccine for patients aged 50 to 59 years, the vaccine is approved by the FDA for, and indicated in, immunocompetent individuals aged 50 years or older.\textsuperscript{6} Research data suggest that the vaccine’s efficacy is greater in younger patients, and that complications (eg, PHN) are decreased in vaccinated persons, compared with unvaccinated persons, in whom herpes zoster develops.\textsuperscript{8,9}

As previously noted, although Zostavax has been shown in multiple studies to be safe for patients younger than 60 years,\textsuperscript{7,9} the ACIP’s lack of recommendation for using the vaccine in that age group is based on supply concerns, on the limited amount of data on long-term duration of response, and on the possible need for a booster 20 to 30 years after the initial vaccine.\textsuperscript{10} From a practical, clinical perspective, however, if a patient aged 50 years or older requests the herpes zoster vaccine, is able to pay for it, and is immunocompetent, the vaccine can be safely administered under FDA indications.

**Next Steps**

If our patients understood their risk of herpes zoster, the impact it could have on their lives, and the fact that herpes zoster could be prevented with a safe vaccine, I believe that many patients would be lining up at our doors to receive it—even if it meant getting a booster in 25 years. We are failing our patients by not advocating more on their behalf, by not educating them about the incidence and severity of shingles in older age groups, and by not strongly recommending vaccination that could prevent severe morbidity in their lives. The economic and psychological burden of herpes zoster in the aging population is substantial—with direct costs related to healthcare and indirect costs related to lost income and function and persistent, chronic, debilitating pain.

Important clinical questions that remain unanswered include the duration of immunity, whether Zostavax can be safely administered to patients who are immunosuppressed by illness (eg, human immunodeficiency virus) or by medications (eg, corticosteroids, chemotherapy), and whether the herpes zoster vaccine can be safely administered with the influenza vaccine. Limited data exist on administration of the herpes zoster vaccine with other inactivated vaccines, but the simultaneous administration of multiple inactivated vaccines is generally accepted and has not been shown to result in impaired immune response.\textsuperscript{7,13}

Postlicensure studies among the established cohorts from the initial trials that led to FDA approval of the herpes zoster vaccine will clarify information about duration of vaccine protection. Additional studies aimed at evaluation of
the vaccine among immunocompromised patients—including individuals with human immunodeficiency virus infection, recipients of transplanted organs, and chronic users of steroids—are anticipated. If supply of the herpes zoster vaccine increases in a sustainable manner, the ACIP may revise its recommendations for the vaccine to include patients aged 50 to 59 years.

References

Peer Reviewers Wanted
Peer reviewers are physicians, basic scientists, and other healthcare professionals who critically evaluate the scientific quality and clinical significance of research submitted to JAOA—The Journal of the American Osteopathic Association for publication. The JAOnA is currently looking for such individuals who are interested in serving as peer reviewers.

For additional information and to complete a form for becoming a JAOnA peer reviewer, visit http://www.jaoa.org/misc/peer.xhtml. Prospective peer reviewers can also contact the JAOnA’s editorial assistant at jaoa@osteopathic.org for more information.