### Vaccine for Herpes Zoster

**Generic (Trade Name):** Zoster vaccine live (Oka/Merck) (Zostavax™)

**Manufacturer:** Merck & Co., Inc.

**Indication:** Zostavax™ is an investigational vaccine for the prevention of shingles (herpes zoster) and shingles-associated nerve pain (postherpetic neuralgia) in adults aged 60 and over.

**Current Regulatory Status:** The Biologics License Application for Zostavax™ is under review by the US Food and Drug Administration (FDA). Merck has also submitted an application for Zostavax™ to Health Canada.¹

**Description:** Shingles is caused by the reactivation of dormant varicella-zoster virus in nerves. This is the virus that causes chicken pox. As immunity to the varicella-zoster virus weakens, for example, with age, the reactivated virus can damage sensory nerve cells, causing pain. It then migrates to the skin, causing the blistering rash of shingles (herpes zoster). The most common complication of shingles is postherpetic neuralgia, a continual, often debilitating nerve pain that can last for months to years.²

Zostavax™ is a preparation of the Oka/Merck strain of live attenuated varicella virus. It is administered as one subcutaneous injection. The minimum potency of the Zostavax™ vaccine is approximately 14 times greater than the minimum potency of Varivax™,³ the vaccine licensed in Canada to prevent chicken pox. This higher potency appears to be required to overcome the age-related decline in cell-mediated immunity to the varicella-zoster virus.⁴ Zostavax™ was developed for use in older adults.⁴

**Current Treatment:** The management of acute herpes zoster infection includes the use of analgesics, to manage pain; and of antiviral agents, such as acyclovir, valacyclovir, and famcyclovir, to shorten the duration of infection, and reduce the incidence and duration of postherpetic neuralgia.⁵ To be effective, antiviral agents must be taken within 72 hours of the onset of the rash. For patients who develop postherpetic neuralgia, tricyclic antidepressants (e.g., amitriptyline, desipramine), anticonvulsants (e.g., gabapentin, pregabalin), opioids, lidocaine patch and topical capsaicin were found to help reduce the pain.⁶⁻⁷⁻⁸

**Cost:** Costing information for Zostavax™ is unavailable.

**Evidence:** Zostavax™ was evaluated in a phase III Shingles Prevention Study, a double-blind, placebo-controlled randomized controlled trial (RCT) involving 38,546 men and women.⁴ Adults who were ≥60 years old were randomized in a 1:1 ratio to receive one dose of either Zostavax™ (0.5 mL) or placebo. During the three-year follow-up period, there were 642 cases of shingles in the placebo group compared with 315 cases in the vaccine group—a 51% relative reduction in the incidence of shingles (95% CI: 44.2 to 57.6;
The “burden of illness” (defined in the study as the severity and duration of pain and discomfort associated with herpes zoster) was also significantly reduced in the Zostavax™ group. Vaccine recipients had a 61% (95% CI: 51.1 to 69.1; p<0.001) relative reduction in this outcome compared with placebo recipients. The trial also showed a 66.5% (95% CI: 47.5 to 79.2; p<0.001) relative reduction in the incidence of postherpetic neuralgia in the Zostavax™ group (27 cases) compared with the placebo group (80 cases).

In the Shingles Prevention Study, safety evaluations were conducted during the first 42 days after vaccination. Results showed that the number and types of serious adverse events (SAEs) in the total study population were similar in the Zostavax™ and placebo groups. SAEs were reported in 255 adults receiving Zostavax™ and 254 adults receiving placebo. Five SAEs were assessed by investigators as being possibly treatment-related. Two of these were in the active vaccine group, and three were in the placebo group.

Approximately 300 individuals at each of the 22 study sites (6,616 adults) were enrolled in an adverse events substudy. The substudy more closely monitored adverse events in the first 42 days after vaccination. The substudy showed that significantly more adults in the Zostavax™ group had injection-site reactions than did adults in the placebo group (48.3% versus 16.6%, p<0.05). Injection-site reactions were generally mild, and included erythema, pain, or swelling. Zostavax™ was also associated with significantly more SAEs compared with placebo (1.9% in the vaccine group versus 1.3% in the placebo group, p=0.03). There were no significant differences in the distribution of these SAEs according to body system or type of event (specific data not provided).

The annual incidence of herpes zoster varies from 2.2 cases to 3.4 cases per 1,000 adults. This incidence increases with age. About 50% of untreated adults with herpes zoster over the age of 60 develop postherpetic neuralgia, and the incidence increases to approximately 75% in untreated adults over the age of 70. Postherpetic neuralgia is especially difficult to treat, and Zostavax™ has proved to be effective in reducing the incidence of this debilitating form of chronic nerve pain. However, it is important to note that these findings stem from only one study. Indeed, the best way to prevent postherpetic neuralgia may be to prevent herpes zoster itself.

References:
1. FDA advisory committee agrees that clinical data support the efficacy and safety of Zostavax™, Merck’s investigational vaccine for shingles, in adults aged 60 and older. Whitehouse (NJ): Merck & Co; 2005. Available:


This series highlights medical technologies that are not yet in widespread use in Canada and that may have a significant impact on health care. The contents are based on information from early experience with the technology; however, further evidence may become available in the future. These summaries are not intended to replace professional medical advice. They are compiled as an information service for those involved in planning and providing health care in Canada.

These summaries have not been externally peer reviewed.

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