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Shingles Vaccine: FAQs

The chart below addresses common clinical questions about the herpes zoster or shingles vaccines (*Shingrix*, *Zostavax* [U.S.], *Zostavax II* [Canada]).

Abbreviations: ACIP = Advisory Committee on Immunization Practices; CDC = Centers for Disease Control and Prevention; FDA = U.S. Food and Drug Administration; NACI = National Advisory Committee on Immunization; NNT = number needed to treat.

<table>
<tr><th>Clinical question</th><th colspan="3">Pertinent information</th></tr>
<tr><td rowspan="5">What are important differences among the available shingles vaccines?</td><td></td><td>Shingrix</td><td>Zostavax (U.S.) and Zostavax II (Canada)</td></tr>
<tr><td>Type of vaccine[c] (live or recombinant)</td><td>Recombinant zoster vaccine (RZV formerly herpes zoster subunit vaccine [HZ/su]), with an adjuvant to boost immunity[13,14]</td><td>Herpes Zoster Live-Attenuated Vaccine (ZVL)[3,5]</td></tr>
<tr><td>Dosage</td><td>Two doses:[13,14] 0.5 mL each
Second dose given two to six months AFTER the first dose.[13,14,e]</td><td>One dose:[3,5] 0.65 mL</td></tr>
<tr><td>Route of administration</td><td>Intramuscular[13,14,d]</td><td>Subcutaneous[3,5]</td></tr>
<tr><td>Injection-site pain</td><td>69% to 86%[13,14,b,d]</td><td>54%[3,5,b]</td></tr>
<tr><td>At what age should the shingles vaccine be administered?

Continued…</td><td colspan="3">• Risk of getting zoster or having prolonged postherpetic neuralgia pain is much lower in patients 50 to 59 years of age than in patients 60 years of age and older.[1]
• *Shingrix* is the preferred shingles vaccine.[2,36,37]
  ○ Vaccination with *Shingrix* is recommended for people 50 years of age and older.[2,13,14,36]
  ○ *Shingrix* (full series) is recommended even in patients that have previously been vaccinated with *Zostavax* (U.S.) or *Zostavax II* (Canada).[2,36]
  ▪ Administer *Shingrix* as early as eight weeks after *Zostavax* (U.S.) [Evidence Level C] (one year after *Zostavax II* [Canada] [Evidence Level C]), but especially if it has been more than five years since *Zostavax* or *Zostavax II* was given, as most of the protection is lost by then.[2,23,27-29,36,37]
• *Zostavax* may be given to healthy adults 60 years of age and older.[1] This may be appropriate for patients allergic to *Shingrix*, if a patient prefers *Zostavax* (e.g., subcutaneous injection), or if a patient requests vaccination and *Shingrix* is unavailable.[36]
• *Zostavax II* is recommended by Canadian guidelines for people 50 years of age and older.[2]</td></tr>
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Clinical question	Pertinent information
Age of administration, continued	• Both *Zostavax* and *Zostavax II* are FDA- and Health Canada-approved for patients 50 years of age and older.[3,5] However, it is uncertain whether vaccination within the age range of 50 to 59 years with these vaccines will provide ongoing protection at older ages when the incidence of zoster and risk of complications is higher.[1,2] (See duration of *Zostavax* and *Zostavax II* immunity below.)
Should patients who've had shingles receive the vaccine?	• Vaccination is recommended regardless of shingles or chickenpox history.[1,2,36] • Different safety concerns are not expected in persons with a history of shingles.[1,2,12]
How long after a shingles episode can the vaccine be given?	• Re-occurrence risk is low for the first 12 to 18 months after shingles due to residual immunity in immunocompetent patients.[10] • **CDC**: A patient with shingles should wait until the acute stage of the illness is over and symptoms have subsided to be vaccinated, as with all vaccines.[1,37] • **NACI**: It is recommended that at least one year elapse between the last shingles episode and zoster vaccination.[2] o Herpes ophthalmicus has recurred following shingles vaccination (*Zostavax II*).[2] ▪ Causality has not been established, but patients should be informed that the risk/benefit is unknown.[2]
Can the shingles vaccine be administered with other vaccines or medications?	• *Zostavax* and *Zostavax II* can be administered with other live and inactivated vaccines.[1] • *Shingrix* can be safely administered with a **non-adjuvanted** seasonal influenza vaccine without compromising efficacy of either vaccine.[14,23,24,37] Co-administration with the adjuvanted flu vaccine *Fluad* has not been studied. There are theoretical concerns about more side effects when giving two adjuvanted vaccines at the same time.[15] However, don't delay vaccination if only *Fluad* is available.[15] If *Fluad* needs to be given with another adjuvanted vaccine (e.g., *Shingrix*), administer at separate sites.[15] o General guidance suggests that recombinant and adjuvanted vaccines (such as *Shingrix*) can be given concomitantly (at separate sites) with other adult vaccines. However, specific CDC and NACI recommendations for co-administration with other inactivated vaccines (e.g., pneumococcal, Tdap) are not available at time of publication.[2,37] • See our CE, *Safe and Appropriate Use of Live Vaccines*, for more on coadministration of vaccines. • When possible, **live** zoster vaccines (*Zostavax, Zostavax II*) should be administered at least 24 hours after discontinuation of an antiviral agent active against herpes viruses (acyclovir, famciclovir, etc). The antiviral should not be restarted for at least 14 days after vaccination.[18] o Theoretically this should not be a concern with *Shingrix*, as it is a recombinant vaccine (e.g., does not contain live virus). However, no data are currently available.

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Clinical question	Pertinent information
How long does immunity last?	***Zostavax* and *Zostavax II*** • In patients 60 years and older, efficacy wanes within the first five years, and protection beyond five years is uncertain.[1] o Efficacy may start to wane one year after vaccination, especially in older age groups (e.g., >65 years of age).[2] o May provide some efficacy up to seven years, but likely less than ten years.[17] o Though studies are ongoing, there is no current recommendation for a booster or revaccination.[1,2] ***Shingrix*** • Immune response appears to be maintained at least nine years after vaccination based on cellular response.[20,21] o It is unclear if this correlates to continued protection against shingles and postherpetic neuralgia.[20,21] • Maintains >90% efficacy regardless of age at least four years after vaccination.[19] o Maintains about 88% efficacy four years after vaccination in patients vaccinated at 70 years of age or older.[7]
How effective is the shingles vaccine?	**Shingles** • *Zostavax*: NNT ~ 59 patients to prevent one case of shingles over about three years in patients over 60 years of age.[3,5,a] • *Shingrix*: NNT ~ 37 patients to prevent one case of shingles over about three years in patients at least 50 years of age.[11] o Clinical trials have NOT been conducted to evaluate the efficacy of *Shingrix* if just one dose is received.[38] o There is insufficient data available from post-hoc analyses to accurately predict the efficacy of *Shingrix* in patients that have only received one dose.[38] **Postherpetic neuralgia** • All available vaccines have an NNT ~ 350 to prevent one case of postherpetic neuralgia over about three years.[7,25]
Who should NOT receive the shingles vaccines? *Continued…*	***Shingrix*** • There are limited data demonstrating safety and efficacy in immunocompromised patients (e.g., human immunodeficiency virus [HIV], post-transplant, malignancies [solid and hematologic]).[14,32-35] o Though U.S. product labeling warns that immunosuppressive therapy may reduce effectiveness, per the CDC *Shingrix* can be given to patients taking low-level immunosuppressive therapy (e.g., less than 14 days' corticosteroid use, prednisone <20 mg daily or its equivalent, topical or inhaled corticosteroid).[13,36,37] o Per NACI, *Shingrix* may be considered for immunocompromised patients 50 years and older on a case-by-case basis.[2] • There are no data available about risk with use in pregnant or breastfeeding women.[13,14] ***Zostavax*** (U.S.) • Do not administer to immunosuppressed patients, such as severely immunocompromised HIV patients; patients with lymphoma, leukemia, or other diseases affecting the immune system; and those taking meds that affect the immune system such as corticosteroids (≥2 weeks of prednisone 20 mg daily [or equivalent]), chemo, or radiation therapy.[1,4] • Defer vaccination for at least one month after discontinuation of immunosuppressive therapy.[16] • Per the CDC *Zostavax* can be given to patients taking low-level immunosuppressive therapy (e.g., less than 14 days'

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Clinical question	Pertinent information

Who should not receive the shingles vaccine, continued	corticosteroid use, prednisone <20 mg daily or its equivalent, topical or inhaled corticosteroid).[37]
	• Do not administer to women who are or may become pregnant.[1]
	  o Women should not become pregnant until at least three months after getting the vaccine.[5]
	Zostavax II (Canada)
	• This vaccine is contraindicated in patients with primary immune deficiency (e.g., disorders of T-cell function) or acquired immune deficiency (e.g., blood dyscrasia, chemotherapy, radiation therapy, organ or stem cell transplant, cancer affecting the bone marrow or lymphatics).[2] Expert consultation is advised in complex cases.[2]
	  o When indicated, the vaccine can be given to patients with complement deficiency, neutropenia, or certain phagocytic defects (e.g., chronic granulomatous disease).[22] All live attenuated viral vaccines are contraindicated in patients with leukocyte adhesion defect, Chediak-Higashi syndrome and other defects in cytotoxic granule release, and in other undefined phagocytic cell defect.[22]
	  o The vaccine may be considered for people on low-level immunosuppressive therapy, such as after less than 14 days' corticosteroid use, prednisone <20 mg daily or its equivalent, topical or inhaled corticosteroid, corticosteroid joint injection, methotrexate ≤0.4 mg/kg/week, azathioprine ≤3 mg/kg/day, or 6-mercaptopurine ≤1.5 mg/kg/day.[22]
	  o The vaccine can be given at least four weeks before immunosuppressive therapy, four weeks after high-dose corticosteroids, or three months after other immunosuppressive drugs (e.g., cyclosporine, chemo).[22]
	  o Consult an immunodeficiency expert if considering vaccination in a patient with HIV or on an anti-TNF biologic.[2]
	• This shingles vaccine is contraindicated during pregnancy.[2]
	  o Women should not become pregnant until at least three months after getting the vaccine.[3]

How is the shingles vaccine reimbursed?	• Reimbursement for *Shingrix* is beginning to be rolled out, as the official recommendations have been published.
	  o Until reimbursement for *Shingrix* is firmly established, discuss the pros and cons of administering *Zostavax* (U.S.) or *Zostavax II* (Canada) versus waiting to administer *Shingrix*.
	U.S.
	• Medicare Part D covers *Zostavax*, but the patient's share varies by plan.[8] It is expected that Medicare Part D will cover *Shingrix* for patients 65 years and older.[40]
	• Private insurance coverage varies.[9]
	• *Zostavax* costs about $212 to use, while *Shingrix* costs about $280 for the two-dose series.[26]
	Canada
	• In Ontario, patients 65 to 70 years of age can receive *Zostavax II* free of charge from their primary care provider.[6]
	  o Otherwise for other patients and provinces, the out-of-pocket cost of *Zostavax II* is about $190.
	• *Shingrix* costs about $265 for the two-dose series.

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Clinical question	Pertinent information
How must the shingles vaccine be stored?	• *Shingrix* (both the lyophilized antigen vial [vaccine] and adjuvant suspension vial [diluent]) should be refrigerated between 36°F and 46° F (2°C and 8°C).[13,14] o Accidental exposure of the lyophilized antigen vial to temperatures between -13°F and 36°F (-25°C and 2°) does not affect vaccine potency.[31] ▪ However, do not use the adjuvant suspension if exposed to temperatures below 32°F (0°C). Exposure to these temperatures may affect the stability of the adjuvant and potentially reduce the potency of the vaccine.[31] o Vaccine should be reconstituted with the diluent provided and used immediately or refrigerated between 36°F and 46° F (2°C and 8°C) and used within six hours.[13,14] • *Zostavax* (U.S.) should be stored frozen between -58°F and +5°F (-50°C and -15°C) in a unit with a separate, sealed freezer.[5] o It may be stored or transported at refrigerator temperatures 36°F and 46°F (2°C and 8°C) for up to 72 hours prior to reconstitution.[5] ▪ Discard any product not used within 72 hours of removal from freezer.[5] o Vaccine should be reconstituted with the diluent provided and administered within 30 minutes of reconstitution.[5] ▪ The diluent can be stored in the refrigerator between 36°F and 46°F (2°C and 8°C) or at room temperature between 68°F and 77°F (20°C and 25°C).[5] • *Zostavax II* (Canada) should be refrigerated at 2°C to 8°C.[3] o The diluent can be stored in the refrigerator between 2°C and 8°C or at room temperature between 20°C and 25°C.[3] o Vaccine should be reconstituted with the diluent provided and administered within 30 minutes of reconstitution.[3]

a. *Zostavax II* product monograph references efficacy data from *Zostavax* trials.
b. *Shingrix* causes more injection site pain; however, *Zostavax* causes more redness and swelling (indirect comparisons).[5,13]
c. *Quillaja saponaria* Molina, fraction 21 (QS-21) and 3-0-desacyl-4-monophosphoryl lipid A (MPL) act as adjuvants to boost immune response.[13,14]
d. It is not necessary to re-administer *Shingrix* if accidentally given subcutaneously instead of intramuscularly. Subcutaneous administration may result in more severe pain compared to intramuscular administration. Some patients indicated that the pain from the subcutaneous injections was severe enough to interfere with normal activity.[30,39]
e. Vaccine series does not need to be restarted if more than six months have elapsed since the first dose before the second dose is given. The second dose should be repeated if given less than four weeks after the first dose.[37]

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Project Leader in preparation of this clinical resource (331201): *Beth Bryant, Pharm.D., BCPS, Assistant Editor (last modified October 2018)*

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