Non-Live Recombinant Herpes Zoster Vaccine (SHINGRIX)

**Bottom Line…**

- **SHINGRIX** is indicated for the prevention of herpes zoster (HZ or shingles) in adults age ≥ 50
- **SHINGRIX** reduces the risk of shingles by 91% (ARR=3.1%, NNT=32) & postherpetic neuralgia (PHN) by ~90% (ARR=0.30%, NNT=333) in 3 yrs.
- **NNT:** For every 333 vaccinated with **SHINGRIX**, 10 shingle cases (age ≥ 50 years) and 1 PHN cases (age ≥ 50 years) were prevented over ~3 yrs.
- **SHINGRIX** demonstrated efficacy for prevention of shingles effective in all age groups 50-80+. **ZOSTAVAX** less effective with increasing age.
- **SHINGRIX** use in patients with a history of shingles has been studied (open-label, non-randomized trial (n=93 patients, age 50-89 yr) for 3 months).
- **OSTER-003** Vaccine can be given after shingles symptoms/ rash resolved ≥1 yr after
- **Cost – $300 for 2 doses given intramuscularly (IM) 2-6 months apart** (can give up to 12 months apart if needed to increase compliance). (Refrigerate 2 to 8°C; Discard if frozen)
- (New Jan/2021 NIH covers for those between 65 & 70 years of age)
- Canadian NACI †18 recommends **SHINGRIX** should be offered to individuals ≥50 yrs without contraindications including:
  - Individuals previously vaccinated with **ZOSTAVAX** or **ZOSTAVAX II**; Re-vaccinate with two doses of RZV at least one year after receiving **ZOSTAVAX**
  - Individuals with a previous episode of herpes zoster disease. Provide two doses of **SHINGRIX** at least one year after herpes zoster episode. ♂
  - Immunocompromised individuals, may be considered on a case-by-case assessment of the benefits vs risks of **SHINGRIX**
- **ZOSTAVAX II** may be considered for immunocompetent individuals ≥50 yrs without contraindications when **SHINGRIX** is contraindicated, unavailable or inaccessible.
- **Advisory Committee on Immunization Practices (ACIP)** recommends **SHINGRIX** as the preferred vaccine for preventing shingles and related complications.
- **ACIP** also recommends **SHINGRIX** (give both of the 2 doses) for adults who previously received **ZOSTAVAX** or **ZOSTAVAX II.**
- Administer **SHINGRIX** as early as 8 wks after **ZOSTAVAX II**, but especially after 5 yrs (as **ZOSTAVAX** efficacy declines over time).
- **Outstanding Questions:** What is the long-term effectiveness?

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**What is **SHINGRIX**?**

- **Herpes Zoster (shingles) vaccine** contains NON-live, recombinant, AS01B adjuvanted herpes zoster vaccine. This vaccine contains antigen glycoprotein E, which is the most abundant antigen in varicella zoster vaccine (VZV) infected cells and the main target for VZV-specific CD4+ T-cell response. This vaccine also includes adjuvant AS01 that helps to elicit an early, high and long-lasting response with less reactogenicity.
- Indicated for prevention of shingles in patients ≥50 yrs. Not for treating shingles, PHN or preventing primary varicella infection.

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**Is **SHINGRIX** effective?**

Two Studies: Efficacy of the Herpes Zoster Subunit Vaccine: in Adults 70 years of age or older (ZOE-70) 2016 & in Older Adults (ZOE-50) 2015

<table>
<thead>
<tr>
<th>Clinical Outcomes (Pooled ZOE-70 &amp; ZOE-50)*</th>
<th>Vaccine %, n = 8250</th>
<th>Placebo %, n = 8346</th>
<th>RRR</th>
<th>ARR</th>
<th>NNT over 3 years</th>
<th>NNH within 7 days</th>
</tr>
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<tbody>
<tr>
<td>Incidence of shingles (overall)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>NNT = 32</td>
<td></td>
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<tr>
<td>Age 70-79 yr</td>
<td>0.30%, n=25</td>
<td>0.40%, n=264</td>
<td>91.3%</td>
<td>3.10%</td>
<td></td>
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<tr>
<td>Age ≥ 80 yr</td>
<td>(n=19,4668)</td>
<td>(n=284,836)</td>
<td>91.4%</td>
<td>3.45%</td>
<td>33 / 3 yrs</td>
<td>29 / 3 yrs</td>
</tr>
<tr>
<td>Year 1</td>
<td>0.02% (n=2,8250)</td>
<td>0.00% (n=83,846)</td>
<td>97.6%</td>
<td>0.97%</td>
<td>103 / 1 yr</td>
<td>136 / 62 y</td>
</tr>
<tr>
<td>Year 2</td>
<td>0.09% (n=7,0039)</td>
<td>0.00% (n=87,0024)</td>
<td>92.9%</td>
<td>0.95%</td>
<td>172 / 63 y</td>
<td>147 / 47 y</td>
</tr>
<tr>
<td>Year 3</td>
<td>0.12% (n=79,736)</td>
<td>0.76% (n=58,761)</td>
<td>84.7%</td>
<td>0.64%</td>
<td>147 / 47 y</td>
<td>147 / 47 y</td>
</tr>
<tr>
<td>Year 4</td>
<td>0.09% (n=77,426)</td>
<td>0.77% (n=56,726)</td>
<td>86.8%</td>
<td>0.65%</td>
<td>147 / 47 y</td>
<td>147 / 47 y</td>
</tr>
</tbody>
</table>

Cost $300 for 2 doses given intramuscularly (IM) 2-6 months apart (can give up to 12 months apart if needed to increase compliance). (Refrigerate 2 to 8°C; Discard if frozen)
What are potential adverse events and drug interactions with HINGRIX? 1-3,5,10,11,12,13

- **Common adverse events include** (compared to placebo):
  - Reactions were transient, with median durations of 2 to 3 days for injection-site reactions, 1 to 2 days for systemic reactions, and 1 to 2 days for grade 3 reactions. Most reactions were considered mild to moderate in intensity.
  - More redness and swelling > 100mm to affected area lasting 1-2 days (NNH=11-12 in 7 days).
  - More systemic reactions that prevented normal activity for 1-2 days (NNH=11 to 25 in 7 days).
  - Injection site reactions: pain, redness, swelling; and systemic reactions: myalgia, fatigue, headache, shivering, fever, GI symptoms.
  - For age > 70, the overall frequency and severity of the reactions did not increase significantly after 2nd dose (8.5%)
  - For ages 50-70, systemic reactions that prevented normal activity were more frequent after 2nd dose (5.7%) than after the first dose (5.9%) in OZEO-50.

- **Interactions:** Can be administered with other live vaccines & inactivated vaccines.
  - Can be given concomitantly with unadjuvanted seasonal influenza vaccine at different injection sites.
  - Must not be mixed with any other products in the same syringe.

What are other potential cautions regarding the use of HINGRIX? 1-3,5

- **Shingrix** is contraindicated if:
  - Patients have a known hypersensitivity to the active substances or to any component of the vaccine.
  - History of chicken pox
  - History of HZ

- **Can Shingrix be used in immunocompromised patients?**
  - Yes, limited data in patients with autologous Haematopoietic Cell Transplant (HCT) & HIV indicate no safety concerns 1-yr post-vaccination.
  - Pregnancy or Breastfeeding is not a contraindication.

Is administration of Shingrix cost effective? 15

- **Shingrix costs ~ $300 for 2 doses.** (New Jan/2021 NIHB covers for those between 65 & 70 years of age)
- **Shingrix was more effective and less expensive than the live attenuated herpes zoster vaccine at all ages and had an incremental cost-effectiveness ratio from $20,038 to $30,084 per quality-adjusted life year compared to no vaccination study, non-pharmaceutical funding.**

What are the Current Vaccination Recommendations for Herpes Zoster Vaccine (Shingrix)? 16,17,18,19

- **NACI 2018:** Canadian NACI recommends Shingrix should be offered to individuals ≥50 yrs without contraindications.
- **USA – ACIP 2017:** preferred vaccine for preventing shingles & related complications for all ≥50 yrs, including those who previously received Zostavax.
- **History of chicken pox:** HSV can be administered (not studied).

How long after a shingles episode can the Herpes Zoster Vaccine be given? 1-3,5

- No official or specific recommendation for Shingrix.
- **Canada:** It is recommended that at least 1 year elapse between the last shingles episode and zoster vaccination. Herpes ophthalmicus has recurred following Zostavax but causality was not established.
- **CDC:** Vaccine can be administered after the acute stage and symptoms/rash have subsided, no specific time frame.
- **History of HZ:** patients can be vaccinated. In theory, prior episodes of HZ immunity & likelihood of recurrences, but observational evidence is contradictory. 20 A recent study reports the risk of recurrence is ↓ for 12 to 18 months after having HZ so vaccination could be delayed by ≥1 year to take advantage of this natural immunity. 20 (Persons with a history of herpes zoster or had herpes zoster vaccination were excluded from ZOE-50 and ZOE-70 trials.)

How is Shingrix supplied? What is the dosage and how is it administered? 1-3,5

- Supplied as 2 vials: (1) single dose lyophilized gE powder and (2) adjuvant suspension vials both refrigerated (2-8°C) and protected from light.
- Reconstitute prior to administration: **Administer vaccine promptly.** If this is not possible, store in refrigerator (2-8°C) and use within 6 hours. Discard if not used within 6 hours. The reconstituted vaccine is an opalescent, colourless to pale brownish liquid. Discard if frozen.
- Before administration: withdraw the reconstituted vaccine into a sterile syringe and attach a new needle to use for the injection.
- 2 doses of 0.5mL each; an initial dose at Month 0 followed by a second dose administered between 2 and 6 month later.
- **Intramuscular (IM) injection only,** preferably in the deltoit muscle.

Uncertainties

- Can the non-live herpes zoster vaccine be effective and safe in frail elderly or immunocompromised patients over the long term? expert opinion says “yes”
- Of those in the vaccinated group who do get shingles, are severity and complications reduced? Is efficacy retained over longer term?
- As more severe PHN is likely the most important issue, to what extent were the more severe/persistent PHN cases prevented?

What are the advantages and disadvantages of Shingrix vs. Zostavax II? 1-3,5

<table>
<thead>
<tr>
<th>Advantages of Shingrix</th>
<th>Disadvantages of Shingrix</th>
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<tbody>
<tr>
<td>Non-live vaccine – option for immunocompromised persons</td>
<td>Higher reactogenicity, more injection site reactions (pain, redness, swelling), systemic reactions (fatigue, myalgia, headache, shivering, fever, GI symptoms)</td>
</tr>
<tr>
<td>Higher efficacy rate (91% vs. 51%), although different patient population studied</td>
<td>More local redness and swelling (&gt;100mm) &amp; Grade 3 systemic reactions (prevents normal activity) that last for an average median of 1-2 days.</td>
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<tr>
<td>Shingrix is more cost-effective</td>
<td>2-dose schedule</td>
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<td>Zostavax II is gelatin &amp; neomycin, which may induce reaction</td>
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Shingles Extras 27,22:

- **Antivirals (e.g. valcyclovir 1g TID or acyclovir 800mg 5x/day) x 7 days $70;** effective in shingles treatment for age >50 if used within 24-72hrs of rash onset.
- See RxFiles Zostavax Q&A. Zostavax discontinued in 2020 and replaced with Zostavax II.
- See RxFiles Chronic Non-Cancer Pain chart for PHN pain treatment (11th Ed, pg 99) → e.g. nortriptyline, gabapentin, opioid, capsaicin.
- See RxFiles Adult Vaccines Chart (11th ed, pg 77).
References: Inactivated Herpes Zoster Vaccine (SHINGRIX)

10 Le, P., Rothberg M. Herpes zoster infection. BMJ. 2019 Jan;364:k5995.