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AUSTRALIAN TECHNICAL ADVISORY GROUP ON IMMUNISATION (ATAGI) | **CLINICAL ADVICE**

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STATEMENT ON THE CLINICAL USE OF ZOSTER VACCINES IN OLDER ADULTS IN AUSTRALIA

The Australian Immunisation Handbook, available at immunisationhandbook.health.gov.au, is being updated to reflect the clinical advice contained in this statement. Please use this statement for clinical practice guidance in the interim period.

Key Points

- There are two zoster vaccines now available for use in adults aged ≥50 years in Australia to prevent herpes zoster (Table 1):
  - **Zostavax** (Merck) is a live-attenuated varicella zoster virus vaccine. Zostavax requires a single dose.
  - **Shingrix** (GlaxoSmithKline) is an adjuvanted recombinant varicella zoster virus glycoprotein E (gE) subunit (non-live) vaccine. Shingrix requires two doses, with an interval of 2-6 months between doses.
- Shingrix is preferred over Zostavax from age 50 years and above for prevention of herpes zoster and its complications, due to its higher efficacy. Shingrix is now available in Australia through private prescription only. It is not available through the NIP.
- Zostavax remains a readily available and effective alternative vaccine for **immunocompetent adults** aged ≥50 years who wish to reduce their risk of herpes zoster. It is recommended and funded under the National Immunisation Program (NIP) for immunocompetent people aged 70 years of age (with catch-up for those aged 71-79 years until October 2023).
- In **immunocompromised adults**, Zostavax is generally contraindicated and Shingrix should be used. However, Zostavax may be given to those with **mild** immunocompromise where Shingrix is not accessible, after careful assessment of the degree of immunocompromise using the 'Live shingles vaccine (Zostavax) screening for contraindications' tool.
- Zostavax recommendations have not changed. For further details regarding the use of Zostavax please refer to the Australian Immunisation Handbook. Providers should also be aware of the recent TGA requirement for a boxed warning in the Zostavax Product Information.
- Shingrix is associated with moderately high rates of local and systemic reactions that generally do not prevent normal activities and resolve within 1-3 days. Providers should counsel recipients on what to expect after vaccination.
- Recipients of Shingrix should be advised that it is necessary to complete the two-dose schedule to ensure an adequate level and duration of protection.

Table 1. Zoster vaccines available for use in Australia in 2021

	Vaccine	
	Zostavax	**Shingrix**
Number of Doses	1 dose subcutaneously	2 doses intramuscularly
Interval between doses	-	2-6 months
Registered age group	≥50 years	≥50 years
Recommended population group(s)	Immunocompetent†	Immunocompetent and Immunocompromised
NIP* funding	70 years*	Not NIP funded

† Zostavax must NOT be administered to significantly immunocompromised people. In people with mild immunocompromise, safety must be assessed on a case-by-case basis using the 'Live shingles vaccine (Zostavax) screening for contraindications' tool. If there is any uncertainty about the level of immunocompromise Zostavax should not be administered.

* NIP: National Immunisation Program. An NIP-funded dose is available for those not previously vaccinated and aged 71-79 years until October 2023.

What is Shingrix vaccine?

- Shingrix is a recombinant varicella zoster virus glycoprotein E (gE) subunit vaccine with AS01B adjuvant. It is not a live vaccine and therefore can be safely used in immunocompromised people.
- A complete course of Shingrix vaccination requires 2 doses of 0.5mL IM. Two doses are necessary to ensure an adequate level and duration of protection. The recommended minimum interval between doses is 2 months. However, an interval of 2 to 6 months between doses is considered acceptable.[1]
- Shingrix has been registered with the Therapeutic Goods Administration (TGA) for adults ≥50 years since 2017 but has been unavailable due to limited global supply.
- Shingrix is now available in Australia through private prescription only. It is not currently funded under the NIP.

Which zoster vaccine should I give?

Immunocompetent adults

- Shingrix is preferred over Zostavax for prevention of herpes zoster and associated complications in immunocompetent adults (please refer to the GRADE assessment of Shingrix on NCIRS' website).
- Both Shingrix and Zostavax have good efficacy in preventing herpes zoster, but they have not been compared in head-to-head clinical trials. Studies of each vaccine against placebo, however, suggest that Shingrix may be substantially more efficacious[2], particularly in the elderly, and offer longer lasting protection against herpes zoster.
    - In two large clinical trials, Shingrix provided 97% protection against herpes zoster in immunocompetent adults ≥50 years and 91% protection in immunocompetent adults ≥70 years.[3, 4] In clinical trials Zostavax efficacy was lower, and decreased with increasing age (70% in people aged 50-59 years, 64% in those aged 60-69 years, 41% in 70-79 years, and 18% in 80-89 years (no longer statistically significant in this age group)).[5, 6]
- High vaccine efficacy has been demonstrated up to 4 years after vaccination with two-doses of Shingrix, and immunogenicity data suggests protection may persist beyond 10 years.[3, 4, 7] In contrast, the effectiveness of Zostavax appears to decrease significantly by 5-10 years after vaccination.[2, 8-10]
- Zostavax remains an effective alternative to Shingrix for the prevention of herpes zoster and associated complications. A single dose of Zostavax is readily available on the NIP for those aged 70 years, and for those up to 79 years via a catch-up program to October 2023.
- Recommendations for Zostavax use are unchanged. Please refer to the Australian Immunisation Handbook for further details. The Handbook will be updated with information from this statement soon.

Immunocompromised adults

- Shingrix is recommended for the prevention of herpes zoster and associated complications in immunocompromised adults (please refer to the GRADE assessment of Shingrix on NCIRS' website).
- Shingrix has been shown to provide good protection against herpes zoster and associated complications in some highly immunocompromised populations for up to 2 years following vaccination.[11, 12] A robust immune response has also been demonstrated in a broader range of immunocompromised populations aged ≥18 years[11-16] However, the vaccine is only registered for use in those aged ≥50 years.
- **Zostavax is contraindicated** in people with current or recent significant immunocompromise due to the risk of disseminated varicella disease from the Oka strain vaccine virus[17].
- Zostavax may be given to those with **mild** immunocompromise, if Shingrix is not accessible, after careful assessment on a case-by-case basis of the degree of immunocompromise using the 'Live shingles vaccine (Zostavax) screening for contraindications' tool. If there is any uncertainty about the level of immunocompromise, Zostavax should not be administered. For further details please refer to the Australian Immunisation Handbook.

What should you consider when offering a zoster vaccine?

While both zoster vaccines are registered and can be given from 50 years of age, it is important to consider several factors when deciding when to offer any zoster vaccine:

- **the age-related risk of HZ and its complications.** The risk of herpes zoster increases from an estimated annual rate of 6 per 1000 in people aged 50–59 years, to 15 per 1000 in people aged 70–79 years.[18] The likelihood of complications such as PHN also increase with age.[18]
- **the duration of protection offered by the vaccine chosen**. Shingrix has demonstrated high vaccine efficacy to 4 years after vaccination, and immunogenicity data suggests protection may persist to at least 10 years.[3, 4, 7] Effectiveness of Zostavax appears to wane more quickly, decreasing significantly by 5-10 years after vaccination.[8-10]
    - It is possible that a person vaccinated at a younger age, e.g. in their 50's or 60's, may have reduced protection from vaccination as they age, when the risk of zoster is higher.
    - There is currently insufficient evidence to inform recommendations for booster doses for either vaccine. Clinical studies will assess the need for booster doses and inform future recommendations by ATAGI.

- **immune status.** Immunocompromised people are at significantly higher risk of herpes zoster and severe complications than immunocompetent people.[19-21] Duration of protection of zoster vaccines in this population is less certain. If there is uncertainty about the optimal timing of vaccination this should be discussed with the patient's specialist.
    - Household contacts (≥50 years of age) of unvaccinated immunocompromised people should also consider receiving zoster vaccination in order to offer some indirect protection against VZV for the immunocompromised household member.[17]
- **personal preferences.** A person's desire to protect themselves from herpes zoster and related complications may vary and this will influence decision-making on when to receive zoster vaccination.

What adverse events can occur after receiving Shingrix?

- Shingrix causes moderately high rates of local and systemic reactions
- Common reactions include: injection-site pain (up to 79%), redness (up to 39%) and swelling (up to 26%) and systemic symptoms such as fatigue and myalgia (up to 46%), headache (up to 39%), shivering (up to 28%), fever (up to 22%), and gastrointestinal symptoms (up to 18%).
- In a small proportion of people (approximately 10%), reactions may be severe enough to disrupt normal daily activities; but these are generally short-lived (1-3 days) and go away without treatment.
- Rates of local and systemic reactions appear to be slightly higher after Shingrix than with Zostavax.
- Prior to vaccination, immunisation providers should counsel people regarding what local and systemic reactions to expect and the importance of completing the two-dose schedule for an adequate level and duration of protection.
- Preliminary US data suggests a possible but very rare risk of Guillain Barre Syndrome (GBS), a demyelinating neurological condition, following Shingrix (an estimated 3-6 additional cases per million doses administered).[22] However, GBS may also be triggered by zoster itself [23], and modelling suggests the overall benefits of vaccination outweigh the risks of GBS.[24]

Can Shingrix be administered concomitantly with other vaccines?

- Trials of concomitant administration of Shingrix with other vaccines (quadrivalent influenza vaccine, Pneumovax and Boostrix) suggest no safety concerns or interference with vaccine immune response.[25-27]
- The safety and efficacy of concomitant administration of Shingrix with COVID-19 vaccines or with the adjuvanted influenza vaccine (Fluad Quad) has not been evaluated.
- ATAGI generally recommends a minimum 7 day interval between COVID-19 vaccine and other vaccines. However, co-administration is considered acceptable in some situations. Please refer to the 'ATAGI clinical guidance on COVID-19 vaccine in Australia' for the most up-to-date information regarding COVID-19 vaccines.
- ATAGI recommends that it is acceptable to co-administer Shingrix and Fluad Quad on the same day if necessary. However, given the lack of co-administration data for these two adjuvanted vaccines, it is preferred to separate their administration by a few days, ensuring that any adverse events following immunisation with the first vaccine have resolved prior to administration of the other vaccine.

Can people who have previously received Zostavax receive Shingrix?

- People who have previously received Zostavax can receive Shingrix if they wish to increase their protection against herpes zoster.
- Shingrix has been demonstrated to be immunogenic and safe in people who had received Zostavax a minimum of 5 years prior.[28, 29]
- ATAGI recommends a minimum interval of at least 12 months between receipt of Zostavax and a subsequent dose of Shingrix. There is an absence of specific data to inform the optimal interval between receipt of Zostavax and Shingrix.

Can people who have experienced a prior episode of herpes zoster receive Shingrix?

- People who have previously experienced herpes zoster are at risk of recurrent episode(s), and can receive Shingrix.[30]
- There is limited evidence for the use of Shingrix in these people, however no safety or immunogenicity concerns have been identified.[31]
- ATAGI recommends delaying vaccination for at least 12 months after an episode of herpes zoster before receiving herpes zoster vaccination.

Contraindications and Precautions to the use of Shingrix

- Shingrix should not be used for the prevention of primary varicella infection (chickenpox). Varicella vaccine should be considered.
- Shingrix should not be used for treatment of acute herpes zoster illness or postherpetic neuralgia.

- There are no data on the use of Shingrix in pregnant or breastfeeding women.
- Do not administer Shingrix to people with a history of anaphylaxis to a previous dose of Shingrix or to any component of Shingrix vaccine.
- Avoid co-administration of Shingrix concomitantly with COVID-19 vaccines.

Please refer to the Therapeutic Goods Administration Product Information for further information on Shingrix.

References

1. Lal H, Poder A, Campora L, Geeraerts B, Oostvogels L, Vanden Abeele C, et al. Immunogenicity, reactogenicity and safety of 2 doses of an adjuvanted herpes zoster subunit vaccine administered 2, 6 or 12 months apart in older adults: Results of a phase III, randomized, open-label, multicenter study. Vaccine. 2018;36(1):148-54.
2. Tricco AC, Zarin W, Cardoso R, Veroniki AA, Khan PA, Nincic V, et al. Efficacy, effectiveness, and safety of herpes zoster vaccines in adults aged 50 and older: systematic review and network meta-analysis. Bmj. 2018;363:k4029.
3. Cunningham AL, Lal H, Kovac M, Chlibek R, Hwang SJ, Diez-Domingo J, et al. Efficacy of the Herpes Zoster Subunit Vaccine in Adults 70 Years of Age or Older. N Engl J Med. 2016;375(11):1019-32.
4. Lal H, Cunningham AL, Godeaux O, Chlibek R, Diez-Domingo J, Hwang SJ, et al. Efficacy of an adjuvanted herpes zoster subunit vaccine in older adults. N Engl J Med. 2015;372(22):2087-96.
5. Schmader KE, Levin MJ, Gnann JW, McNeil SA, Vesikari T, Betts RF, et al. Efficacy, Safety, and Tolerability of Herpes Zoster Vaccine in Persons Aged 50-59 Years. Clinical infectious diseases. 2012;54(7):922-8.
6. Oxman MN, Levin MJ, Johnson GR, Schmader KE, Straus SE, Gelb LD, et al. A Vaccine to Prevent Herpes Zoster and Postherpetic Neuralgia in Older Adults. The New England journal of medicine. 2005;352(22):2271-84.
7. Hastie A, Catteau G, Enemuo A, Mrkvan T, Salaun B, Volpe S, et al. Immunogenicity of the Adjuvanted Recombinant Zoster Vaccine: Persistence and Anamnestic Response to Additional Doses Administered 10 Years After Primary Vaccination. The Journal of infectious diseases. 2020.
8. Morrison VA, Johnson GR, Schmader KE, Levin MJ, Zhang JH, Looney DJ, et al. Long-term persistence of zoster vaccine efficacy. Clin Infect Dis. 2015;60(6):900-9.
9. Schmader KE, Oxman MN, Levin MJ, Johnson G, Zhang JH, Betts R, et al. Persistence of the efficacy of zoster vaccine in the shingles prevention study and the short-term persistence substudy. Clin Infect Dis. 2012;55(10):1320-8.
10. Tseng HF, Harpaz R, Luo Y, Hales CM, Sy LS, Tartof SY, et al. Declining Effectiveness of Herpes Zoster Vaccine in Adults Aged ≥60 Years. J Infect Dis. 2016;213(12):1872-5.
11. Bastidas A, de la Serna J, El Idrissi M, Oostvogels L, Quittet P, Lopez-Jimenez J, et al. Effect of Recombinant Zoster Vaccine on Incidence of Herpes Zoster After Autologous Stem Cell Transplantation: A Randomized Clinical Trial. JAMA. 2019;322(2):123-33.
12. Dagnew AF, Ilhan O, Lee WS, Woszczyk D, Kwak JY, Bowcock S, et al. Immunogenicity and safety of the adjuvanted recombinant zoster vaccine in adults with haematological malignancies: a phase 3, randomised, clinical trial and post-hoc efficacy analysis. Lancet Infect Dis. 2019;19(9):988-1000.
13. Vink P, Delgado Mingorance I, Maximiano Alonso C, Rubio-Viqueira B, Jung KH, Rodriguez Moreno JF, et al. Immunogenicity and safety of the adjuvanted recombinant zoster vaccine in patients with solid tumors, vaccinated before or during chemotherapy: A randomized trial. Cancer. 2019;125(8):1301-12.
14. Vink P, Ramon Torrell JM, Sanchez Fructuoso A, Kim SJ, Kim SI, Zaltzman J, et al. Immunogenicity and Safety of the Adjuvanted Recombinant Zoster Vaccine in Chronically Immunosuppressed Adults Following Renal Transplant: A Phase 3, Randomized Clinical Trial. Clin Infect Dis. 2020;70(2):181-90.
15. Stadtmauer EA, Sullivan KM, Marty FM, Dadwal SS, Papanicolaou GA, Shea TC, et al. A phase 1/2 study of an adjuvanted varicella-zoster virus subunit vaccine in autologous hematopoietic cell transplant recipients. Blood. 2014;124(19):2921-9.
16. Berkowitz EM, Moyle G, Stellbrink HJ, Schurmann D, Kegg S, Stoll M, et al. Safety and immunogenicity of an adjuvanted herpes zoster subunit candidate vaccine in HIV-infected adults: a phase 1/2a randomized, placebo-controlled study. J Infect Dis. 2015;211(8):1279-87.
17. Australian Technical Advisory Group on Immunisation. Australian Immunisation Handbook. 2018. Department of Health; Available from: https://immunisationhandbook.health.gov.au/vaccine-preventable-diseases/zoster-herpes-zoster#expand-collapse-all-top.
18. MacIntyre R, Stein A, Harrison C, Britt H, Mahimbo A, Cunningham A. Increasing trends of herpes zoster in Australia. PLoS One. 2015;10(4):e0125025.
19. Liu B, Heywood AE, Reekie J, Banks E, Kaldor JM, McIntyre P, et al. Risk factors for herpes zoster in a large cohort of unvaccinated older adults: a prospective cohort study. Epidemiol Infect. 2015;143(13):2871-81.
20. Qian J, Heywood AE, Karki S, Banks E, Macartney K, Chantrill L, et al. Risk of Herpes Zoster Prior to and Following Cancer Diagnosis and Treatment: A Population-Based Prospective Cohort Study. J Infect Dis. 2019;220(1):3-11.
21. Forbes HJ, Bhaskaran K, Thomas SL, Smeeth L, Clayton T, Langan SM. Quantification of risk factors for herpes zoster: population based case-control study. Bmj. 2014;348:g2911.
22. US Food & Drug Administration. Risk of Guillain-Barré syndrome (GBS) following Recombinant Zoster Vaccine (RZV). 2021. CDC; Available from: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-02/24-25/02-Zoster-Vaccines-Forshee.pdf.
23. Kang J-H, Sheu J-J, Lin H-C. Increased Risk of Guillain-Barré Syndrome following Recent Herpes Zoster: A Population-Based Study across Taiwan. Clinical Infectious Diseases. 2010;51(5):525-30.
24. Prosser L. Projected Risks and Health Benefits of Vaccination against Herpes Zoster and Related Complications: Interim Results. 2021. CDC; Available from: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-02/24-25/03-Zoster-Vaccines-Prosser.pdf.
25. Maréchal C, Lal H, Poder A, Ferguson M, Enweonye I, Heineman TC, et al. Immunogenicity and safety of the adjuvanted recombinant zoster vaccine co-administered with the 23-valent pneumococcal polysaccharide vaccine in adults ≥50 years of age: A randomized trial. Vaccine. 2018;36(29):4278-86.
26. Strezova A, Lal H, Enweonye I, Campora L, Beukelaers P, Segall N, et al. The adjuvanted recombinant zoster vaccine co-administered with a tetanus, diphtheria and pertussis vaccine in adults aged ≥50 years: A randomized trial. Vaccine. 2019;37(39):5877-85.
27. Schwarz TF, Aggarwal N, Moeckesch B, Schenkenberger I, Claeys C, Douha M, et al. Immunogenicity and Safety of an Adjuvanted Herpes Zoster Subunit Vaccine Coadministered With Seasonal Influenza Vaccine in Adults Aged 50 Years or Older. The Journal of infectious diseases. 2017;216(11):1352-61.
28. Grupping K, Campora L, Douha M, Heineman TC, Klein NP, Lal H, et al. Immunogenicity and Safety of the HZ/su Adjuvanted Herpes Zoster Subunit Vaccine in Adults Previously Vaccinated With a Live Attenuated Herpes Zoster Vaccine. The Journal of infectious diseases. 2017;216(11):1343-51.
29. Dagnew AF, Klein NP, Hervé C, Kalema G, Di Paolo E, Peterson J, et al. The Adjuvanted Recombinant Zoster Vaccine in Adults Aged ≥65 Years Previously Vaccinated With a Live-Attenuated Herpes Zoster Vaccine. The Journal of infectious diseases. 2020.
30. Yawn BP, Wollan PC, Kurland MJ, St Sauver JL, Saddier P. Herpes zoster recurrences more frequent than previously reported. Mayo Clin Proc. 2011;86(2):88-93.
31. Godeaux O, Kovac M, Shu D, Grupping K, Campora L, Douha M, et al. Immunogenicity and safety of an adjuvanted herpes zoster subunit candidate vaccine in adults ≥ 50 years of age with a prior history of herpes zoster: A phase III, non-randomized, open-label clinical trial. Hum Vaccin Immunother. 2017;13(5):1051-8.