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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 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 available for adults in Australia to prevent herpes zoster (Table 1):
    - **Zostavax** (Merck) is a live-attenuated varicella zoster virus vaccine. Zostavax requires a single dose and is registered for use from age ≥50 years.
    - **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. It is registered for use from age ≥50 years in immunocompetent adults and from age ≥18 years for immunocompromised individuals at increased risk of herpes zoster. A shorter interval of 1-2 months between doses is acceptable in individuals who are currently or shortly expected to be immunocompromised.
- In those aged 50 years and above, Shingrix is preferred over Zostavax for prevention of herpes zoster and its complications, due to its higher efficacy. Shingrix is available in Australia through private prescription only. It is not currently available through the NIP.
- In **immunocompetent adults** aged ≥50 years, Zostavax remains a readily available and effective alternative vaccine to reduce the 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 aged 18-49 years**, Shingrix is the only vaccine available to prevent herpes zoster.
- In **immunocompromised adults aged ≥50 years**, 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 boxed warning in the Zostavax Product Information regarding contraindications for use in those who are severely immunocompromised and the need for a pre-screening risk-based assessment to be completed before administration. (https://immunisationhandbook.health.gov.au/resources/handbook-tables/table-live-shingles-vaccine-zostavax-screening-for-contraindications)
- 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.
- There is currently insufficient evidence to inform recommendations for booster doses for either zoster vaccine.
- Co-administration of COVID-19 vaccine, other vaccines and Zoster vaccines is acceptable if required. There is the potential for an increase in mild to moderate adverse events when more than one vaccine is given at the same time. Separation of Shingrix from other vaccines may be preferable where possible.

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 (immunocompetent) 1-6 months‡ (immunocompromised)
Registered age group	≥50 years	≥50 years (immunocompetent)

	Vaccine	
		≥18 years (immunocompromised)
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.

‡ A shorter interval of 1-2 months can be considered to provide more rapid protection in immunocompromised individuals.

* 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] A shorter interval of 1-2 months can be used in individuals who are currently or shortly expected to be immunocompromised.
- Shingrix has been registered with the Therapeutic Goods Administration (TGA) for adults ≥50 years since 2017. In late 2021, registration was expanded to include immunocompromised individuals aged ≥18 years at increased risk of herpes zoster.
- 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 aged ≥50 years (please refer to the GRADE assessment of Shingrix on the 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 the NCIRS website).
- Shingrix can be given from age 18 years if there is immunocompromise and an increased risk of herpes zoster; however, consideration should be given to the most appropriate age to vaccinate given uncertainties about the duration of protection (see below).
- Shingrix has been shown to provide good protection against herpes zoster and associated complications in some highly immunocompromised populations aged ≥18 years for up to 2 years following vaccination.[11] Longer term data are awaited. A robust immune response has also been demonstrated in a broader range of immunocompromised populations aged ≥18 years[11-16]
- **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?

Both zoster vaccines are registered and can be given from 50 years of age. For those aged 18-49 years, only Shingrix is registered, for those with increased risk of herpes zoster due to immunocompromise. It is important to consider several factors when deciding when to offer any zoster vaccine:

- **the age-related risk of herpes zoster and its complications.** The risk of herpes zoster increases with age; the estimated annual incidence rate in the general population is 4.6 per 1000 people aged 25-49 years, 6 per 1000 between 50–59 years, increasing to 15 per 1000 between 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 in immunocompetent adults, 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. However, the absolute risk varies and may still be low in some younger immunocompromised people compared to the healthy elderly.[19-22] Data on the duration of protection of zoster vaccines in this population is limited. 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%), 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.
- US data suggests a possible but very rare risk of Guillain Barre Syndrome (GBS), a demyelinating neurological condition, following Shingrix (an estimated 3 additional cases per million doses administered).[23] However, GBS may also be triggered by zoster itself [24], and modelling suggests the overall benefits of vaccination outweigh the risks of GBS.[25]

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.[26-28]
- 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.
- Co-administration of Shingrix with a COVID-19 vaccine or other vaccines is acceptable based on first principles, if required. There is the potential for an increase in mild to moderate adverse events when more than one vaccine is given at the same time. 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, in the absence of data with Shingrix and specific COVID-19 vaccines, or between Shingrix and Fluad Quad (both adjuvanted vaccines), where possible it may be preferable to separate their administration by a few days, to

ensure 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.[29,30]
- 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.[31]
- There is limited evidence for the use of Shingrix in these people, however no safety or immunogenicity concerns have been identified.[32]
- ATAGI recommends that for immunocompetent individuals vaccination should be delayed for at least 12 months after an episode of herpes zoster before receiving herpes zoster vaccination, as they may benefit from a boost to natural immunity during this time, with some studies suggesting lower recurrence rates in in the first 12 months after the first episode of herpes zoster.[33]
- Immunocompromised individuals are at higher risk of recurrence of zoster[19-22] than immunocompetent individuals and can receive Shingrix from 3 months after the acute illness. Vaccination soon after an acute episode should be balanced by considerations regarding the uncertainty about the duration of protection of Shingrix in immunocompromised individuals, and the absence of recommendations for booster doses after the initial course.

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.
- Co-administration of Shingrix concomitantly with COVID-19 vaccines or other vaccines is acceptable but providers should be aware of the potential for an increase in mild-moderate adverse events

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

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