PHARMAC
TE PĀTAKA WHAIORANGA

# PHARMACEUTICAL SCHEDULE APPLICATION

**To:** Immunisations Advisory Committee

**From:** Funding Application Advisor

**Date:** May 2022

## Recombinant varicella zoster virus glycoprotein E (SHINGRIX) for the prevention of herpes zoster (HZ) and post-herpetic neuralgia (PHN) for adults aged 65 years and over [P-001780]

| SUMMARY OF PHARMACEUTICAL | | | |
|---|---|---|---|
| **Brand Name** | Shingrix | **Chemical Name** | Recombinant Varicella Zoster Virus glycoprotein E antigen |
| **Indications** | the prevention of herpes zoster and post-herpetic neuralgia in adults 65 years of age or older. | **Presentation** | Powder and suspension for injection. Single pack presentation (containing 1 vial for the antigen and 1 vial for the Adjuvant System) |
| **Therapeutic Group** | Immunisation | **Dosage** | 50mcg gE antigen/0.5mL. Two doses of 0.5mL each, administered 2-6 months apart. |
| **Supplier** | GlaxoSmithKline NZ Ltd | **Application Date** | April 2022 |
| **MOH Restrictions** | Prescription Medicine | **Proposal type** | New listing |
| **Current Subsidy** | NA | **Proposed Restriction** | Special Authority |
| **Proposed Subsidy** | TBC | **Approved by Medsafe for this indication** | Yes |
| **Market Data** | Year 1 | Year 2 | Year 3 |
| **Number of Patients†** | 50,000 | 50,000 | 50,000 |

DHBs, District health board; MOH, Ministry of Health; NPV, Net Present Value.
†Pharmac estimate.

## QUESTIONS TO MEMBERS

*Note to members: These questions have been identified by Pharmac staff as being particularly relevant to the application. Please feel free to provide additional information as appropriate.*

### Need

1. If the currently funded vaccination against herpes zoster (Zostavax) was discontinued, does the Committee consider there would be an unmet health need? If so, why?
2. How severe is the health need of patients with herpes zoster? Please describe the health need of a person with a condition over their lifetime on current treatment.

   2.1. What is the strength and quality of evidence for these needs?
3. What are the health needs of families and whānau of people with herpes zoster (including long-term effects) or of wider society? How severe are these needs?

   3.1. What is the strength and quality of evidence for these needs?
4. Does herpes zoster disproportionally affect:
   - Māori?
   - Pacific people?
   - Other groups already experiencing health disparities relative to the wider New Zealand population (eg. NZ Dep 9-10 deprivation, refugees/asylum seekers)?

   4.1. What is the strength and quality of evidence?
5. Does the Committee consider that the results from Turner et al. to be valid ie the burden of HZ cases seen in primary care has indicates there to be a slightly lower incidence of HZ in Māori compared to other ethnicities?

   5.1. If so, does the Committee consider this could be the result of inequities in access to primary care, or underdiagnosis?

### Health benefit

6. Does the recombinant zoster vaccine provide any additional health benefit or create any additional risks compared with the currently funded live attenuated zoster vaccine? If so, what benefits, or risks are different from the currently funded live attenuated zoster vaccine?

   6.1. What is the strength and quality of any such evidence?

   6.2. What is the duration of benefit of the recombinant zoster vaccine compared to the currently funded live attenuated vaccine, noting that efficacy declines with age?
7. If the recombinant zoster vaccine were to be funded, are there any groups who had previously received the currently funded vaccine that would benefit from vaccination with the recombinant vaccine?
   - If so, how many doses of recombinant vaccine should they receive?
   - How soon after vaccination with the live attenuated zoster vaccine should they receive the recombinant vaccine?

8. Would people contraindicated to the currently funded live attenuated vaccine (eg immunocompromised) benefit from vaccination with the recombinant zoster vaccine if it were to be funded?

9. Which patient population would benefit most from the recombinant zoster vaccine if it were to be funded?

10. What does the Committee consider to be age group that would benefit most (eg 65 years of age [currently eligible], 65 years and over, or 50 years and over as per the Medsafe approved indication)?

    10.1. Should there be a catch-up programme for people who have received a primary course of live attenuated zoster vaccine?

    - How long should any catch-up programme run for?
    - What additional impact would a catch-up programme have on the healthcare system?

    10.2. If the recombinant vaccine were to be funded from age 50, would there be durability of response, or would those individuals have to be vaccinated again later in life? If so, after what period?

11. Does the Committee consider that Māori and Pacific peoples would benefit from access at an earlier age, taking into account the smaller proportion of the Māori and Pacific population that is 65 years and older and lessened life expectancy compared with the wider New Zealand population?

    11.1. If so, from what age should Māori and Pacific peoples be eligible?

    11.2. Does the Committee consider that ethnicity-based access criteria would have a real prospect of improving access for Māori and Pacific peoples?

    11.3. Does the Committee consider there are any reasonable alternatives to ethnicity-based criteria that could improve access for Māori and Pacific peoples?

    - Is there any evidence to support age or equity-based criteria for these population groups?

12. What is the strength and quality of evidence, including its relevance to NZ, for health benefits that may be gained from vaccination with recombinant zoster vaccine? Please provide a high-level appraisal of the evidence (eg study design, population, endpoints).

13. Would the recombinant zoster vaccine produce a health benefit for family, whānau or wider society, additional to the health benefits for people vulnerable to HZ? If so how, and what is the strength and quality of evidence for this benefit?

14. If the recombinant zoster vaccine were to be funded, are there any consequences to the health system that have not been noted in the application or in this paper?

**Suitability**

15. Are there any non-clinical features of the recombinant zoster vaccine (eg dosing schedule) that may impact on use, either by the patient, by family, or by healthcare workers, that have not been considered in the application?

## Costs and savings

16. Does the information in the PICO table (Table 4) accurately reflect the intended population, intervention, comparator and outcome, if vaccination with recombinant zoster vaccine were to be funded for people aged 65 years and over? If not, how should this be adjusted?

17. Would the use of vaccination with recombinant zoster vaccine create any significant changes in health-sector expenditure other than for direct treatment costs (eg diagnostic testing, nursing costs or treatment of side-effects)?

    17.1. Does the committee consider vaccination with recombinant zoster vaccine will result in different rates of inpatient and outpatient events compared with currently funded vaccination?

    17.2. Does the committee have any insight into how primary and secondary dose administration costs could be mitigated? (ie administered with other regular vaccinations required by the target population)

## General

18. Is there any data or information missing from the application, in particular clinical trial data and commentary?

## Recommendations

19. Should the recombinant zoster vaccine (Shingrix) be listed in the Pharmaceutical Schedule?

    - Name the Factors for Consideration particularly relevant to a positive or negative recommendation and explain why each is relevant.

20. If listing is recommended, what priority rating would you give to this proposal within the context of vaccines and immunisation? **[low / medium / high / only if cost-neutral]**?

21. Does the Committee have any recommendations additional to the application?

## PURPOSE OF THIS PAPER

The purpose of this paper is to seek advice from the Committee regarding an application from GSK for the use of recombinant varicella zoster virus glycoprotein E (SHINGRIX) for the prevention of herpes zoster (HZ) and post-herpetic neuralgia (PHN) for adults aged 65 years and over.

## DISCUSSION

### BACKGROUND

*Previous consideration of treatments for herpes zoster vaccines*

In 2017, Pharmac entered an agreement with Merck Sharp & Dohme (New Zealand) Limited to list Zostavax, a lyophilized preparation of a live attenuated varicella vaccine zoster virus, for those aged 65 years and older with a 2-year catch-up programme for people aged between 66 and 80 years inclusive. The clinical advice associated with this proposal is summarised in Table 1 below.

**Table 1:** Clinical advice relating to the listing of Zostavax

| Date | Committee and recommendation | Discussion |
|---|---|---|
| August 2014 | PTAC - Medium | • PTAC noted that evidence for the durability of the vaccine was weak.<br>• The Committee noted that further data on the durability of vaccine may arise from case-control studies with longer follow-ups.<br>• The Committee noted that shingles and PHN have high levels of morbidity particularly for the elderly and can be life-changing, as some patients do not recover well enough to return to independent living and require rest home care. The Committee noted that acute treatment of zoster is difficult as many patients present late and it is difficult to treat PHN in the elderly as it is difficult to achieve satisfactory pain relief. |
| February 2015 | Immunisation Subcommittee - Recommended for funding with no priority | • The Subcommittee noted that PTAC requested that CUA modelling assumptions include a waning of vaccine efficacy over time as per currently available data, and that sensitivity analysis include a possible booster at 10 years (although members did recognise that the 10-year boosted scenario has no current evidence base).<br>• The Subcommittee noted that the zoster vaccination provided good protection for at least 5 years but ongoing immunity is not clear. The Subcommittee noted there was no evidence or information on the need for booster vaccinations.<br>• The Subcommittee noted that zoster vaccine efficacy does vary by age with vaccine efficacy for herpes zoster, at approximately 64% in the 60-69 year age group, 41% in the 70-79 year age group and 18% in the over 80 year age group.<br>• The Subcommittee noted that further analysis and research should be undertaken to ensure that Maori and Pacific Island patients receive equal benefits from funded Zoster vaccination at age 65 considering their age of death is lower than the rest of the population |

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|---|---|---|
| August 2015 | PTAC - Medium | • The Committee reviewed a PHARMAC generated paper on the cost-utility analysis (CUA) of zoster vaccination.<br>• The Committee noted that there was a significant difference in the efficacy of herpes zoster vaccination dependent of the age of vaccination with efficacy of ~64% in 60-69 year olds dropping to 38% in those 70 plus.<br>• The Committee noted the Immunisation Subcommittee had not recommended a booster dose as the Subcommittee had considered that there was no evidence or information on the need for a booster vaccination at this stage. The Committee noted there have been no controlled clinical trials using booster vaccinations and considered there was no need to model a booster dose until the evidence becomes available.<br>• The Committee noted that while Zostavax is registered for use from age 50, the major clinical trials did not include patients under the age of 60 years. The Committee considered 65 was a reasonable age as that coincided with influenza vaccination however it is important to note that that efficacy decreases markedly with age.<br>• The Committee noted long-term follow-up evidence which reported that statistically significant vaccine efficacy for herpes zoster burden of illness persisted into year 10 post vaccination; whereas statistically significant vaccine efficacy for incidence of herpes zoster persisted only through year 8.<br>• The Committee considered that zoster vaccination at 65 years with a catch-up was the best option. The Committee recognised that while the vaccine may be more efficacious in younger age groups, there would be a significant cost associated with these age groups due to the larger numbers of people that could be vaccinated. The cost of vaccination outweighs the benefits in these age groups. |
| February 2016 | PTAC – Medium | • The Committee recommended zoster vaccination be listed on the Pharmaceutical schedule for vaccination of people aged 65 **with a 2 year catch-up programme for people aged between 65 and 80 years with a low priority.**<br>• The Committee recommended zoster vaccination be listed on the Pharmaceutical schedule for vaccination of people **aged 65 with no catch up programme with a medium priority.**<br>• Members considered that the vaccine is less likely to be effective in older people, however if it is effective then older people are likely to receive greater absolute health benefit from the vaccine (because of the dominance of higher case morbidity with age).<br>• The Committee reiterated that it considered 65 was a reasonable age as that coincided with influenza vaccination.<br>• The Committee considered that determining the optimal age(s) of vaccination and catchup programmes is largely a financial decision that has to take into account budget impact and the cost utility analysis. Members noted the significant budget impact of a broad catch-up programme and that it may be unlikely to be affordable due to the |

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| | | poorer cost effectiveness and high cost of the vaccine. The Committee considered that a 2-year catch-up programme for all patients over the age of 65 would be appropriate but would be a lower priority than funding the vaccine for people aged 65 with no catch-up programme, because of these factors. |

Pharmac has not previously received a funding application for Shingrix.

## Need

### Description of the disease

Varicella zoster virus (VZV) is a human alpha-herpes virus that causes varicella during primary infection, establishes latency in sensory neurons, and causes HZ when reactivated. Viral reactivation is associated with impaired immunity – either due to immunosenescence, a natural age-related decline in immune system function, or an underlying immunodeficiency.

During primary infection, VZV particles from skin lesions enter sensory nerves and migrate through primary afferent nerve tissue to become latent in cranial nerve ganglia, dorsal root ganglia and autonomic ganglia along the entire neuraxis.

While latent VZV is non-infectious, it can reactivate in sensory neurons to form virions which can spread from a single ganglion to neural tissue and the associated dermatome and cause HZ.

The infection is usually limited to a single dermatome and the characteristic rash is the result of neurological damage due to viral replication in sensory ganglia causing destruction of the neurons and satellite cells.

### Epidemiology

According to the Ministry of Health Immunisations Handbook (2020), HZ hospitalisations during 2018/2019 were primarily those aged 60 years and over (60% of total 483 hospitalisations). The Ministry of Health (MoH) note that hospitalisations are predicted to account for only a very small proportion of the overall zoster cases as most are managed in primary care.

MoH reports that analysis of general practice electronic records reported the incidence of zoster in New Zealand to be similar (approximately 5 per 100,000 patient-years rising to 12.8 per 100,000 in those aged 80–90 years) to the global incidence estimates.

The supplier has indicated that the risk of developing PHN after HZ varies from 5% to ≥30%, and that herpes zoster ophthalmicus (HZO) develops in 10–25% of individuals with HZ. The rate of complications (including vision loss) associated with HZO is 50–90%.

Data from North America, Europe and Asia-Pacific, mortality rates associated with HZ were found to be 0.02–0.47 per 100,000 person-years, with most deaths occurring in adults ≥60 years of age.

**The health need of the person**

Populations at increased risk for developing HZ are those with decreased immune function, including older adults or individuals who are immunocompromised. Although HZ can affect individuals at a younger age, this occurs less frequently and is usually associated with less severe disease. People with chronic conditions, such as diabetes mellitus and chronic obstructive pulmonary disease (COPD) and immunocompromised individuals of any age are also at increased risk of developing HZ. Immunocompromised patients are also more likely to develop recurrent HZ compared with immunocompetent patients.

The initial presentation of HZ includes the onset of acute neuropathic pain and a unilateral rash of itchy, contagious blisters, most frequently occurring on the chest and face, which typically heals in 2–4 weeks. Pain is the most common symptom of HZ. Other non-pain related complications include keratitis, uveitis/iritis, corneal ulceration, conjunctivitis, choroiditis, oculomotor palsy, optic atrophy, retinitis, acute and chronic glaucoma, and potential cranial nerve complications can also lead to impaired hearing and stroke. Other complications include acute VZV encephalitis, myelitis, post-herpetic pruritus (itch), Ramsay Hunt syndrome, cutaneous disseminated disease, and visceral disseminated disease (without skin involvement).

VZV reactivation in the cerebral arteries has also been shown to directly cause pathological vascular remodelling and ischaemic or haemorrhagic stroke (VZV vasculopathy).

Health related quality of life (HRQoL) studies have highlighted the impact of HZ on patients. In one study, the Zoster Brief Pain Inventory was used to measure severity of pain and interference with activities of daily living because of pain, and the EuroQol EQ-5D assessment tool was used to measure quality of life. The study reported that acute herpes zoster interfered in all health domains, especially sleep (64% of participants), enjoyment of life (58%) and general activities (53%) with a median pain duration of 32.5 days. 24% of the participants had postherpetic neuralgia (PHN) (pain for more than 90 days after rash onset). Anxiety and depression, enjoyment of life, mood and sleep were most frequently affected during the postherpetic neuralgia period (Drolet et al. CMAJ. 2010;182:1731-6).

Another study investigated the impact of an entire episode of HZ or post-herpetic neuralgia (PHN) on an individual's quality of life. Participants were those aged 50 years or older who had painful HZ in the previous 5 years, who completed a survey to evaluate their previous HZ/PHN episode. Generally, pain and QoL outcomes were similar irrespective of when HZ was diagnosed (≤12 versus 13-60 months) and age (50-59 versus ≥60 years). Mean pain scores were significantly higher in those with PHN versus HZ both on average (7.2 versus 6.4) and at worst (8.3 versus 7.4). PHN had a significantly higher impact on patients' perception of their overall QoL, with 37% reporting a high impact (HZ: 19%). Pain restrictions in the following QoL domains significantly impacted on the respondents' perception of QoL: enjoyment of life (level of impact, 31%), general activity (29%), mood (25%), sleep (8%) and walking ability (8%) and were significantly higher in those with PHN than in those with HZ. Sleep was the area worst affected (Lukas et al. Z Gesundh Wiss. 2012;20:441-51).

**HZ and COVID-19**

Newly published research from the US has reported an increased risk of HZ in adults ≥50 years old diagnosed with COVID-19 (Bhavsar et al. Open Forum Infect Dis. 2022;9:ofac118). The study reported that people 50 years and older who had contracted COVID-19 were 15% more likely to develop HZ compared to those who were never diagnosed with COVID-19, and that the risk of HZ was elevated for up to six months after a COVID-19 diagnosis. Those hospitalised for COVID-19 were also reported to be 21% more likely to develop HZ.

**The availability and suitability of existing medicines, medical devices and treatments**

Currently Zostavax, a live attenuated zoster vaccine, is available in New Zealand for those aged 65 years and over. The efficacy of the current zoster vaccine decreases with age, and has demonstrated ~50% efficacy against HZ in adults ≥60 years, and has further reduced efficacy in preventing HZ in older patients (≥70 years), who are at higher risk for both HZ and PHN (Oxman et al. N Engl J Med. 2005;352:2271-84).

Live zoster vaccine is contraindicated in individuals who are immunocompromised, specifically those with immunodeficiency due to haematological malignancies, acquired immune deficiency syndrome (AIDS) or clinical manifestations of human immunodeficiency virus (HIV) infection, and in patients receiving immunosuppressive medical therapy.

In New Zealand, careful pre-administration screening is required by vaccinators to ensure live zoster vaccine is suitable for each patient. The supplier has stated that patients about to commence immunosuppressant therapy, serology tests are required prior to administering live zoster vaccine, which is additional compliance for the vaccinator to manage. However, Pharmac staff note that the Immunisation Advisory Centre states that anyone needing Zostavax should be vaccinated at least one month before commencing immunosuppressive treatment.

**The health need of family, whānau, and wider society**

Both HZ and PHN impact patient's family and whānau, with patients and whānau reporting feeling isolated and having reduced communication during the time of illness (Lukas et al. Z Gesundh Wiss. 2012;20:441-51). Some patients do not recover enough to return to independent living resulting in significant carer burden for caregivers of patients including partners, relatives, whānau and friends (Scott et al. Vaccine. 2006;24:1308-14). Patients may also not be able to continue to work, which can further impact burden on partners and family.

**The impact on the Māori health areas of focus and Māori health outcomes**

Research published in 2021 reported that Māori are 2.5 times more likely to be admitted to hospital with COVID-19 than non-Māori (Steyn et al. N Z Med J. 2021;134:28-43).

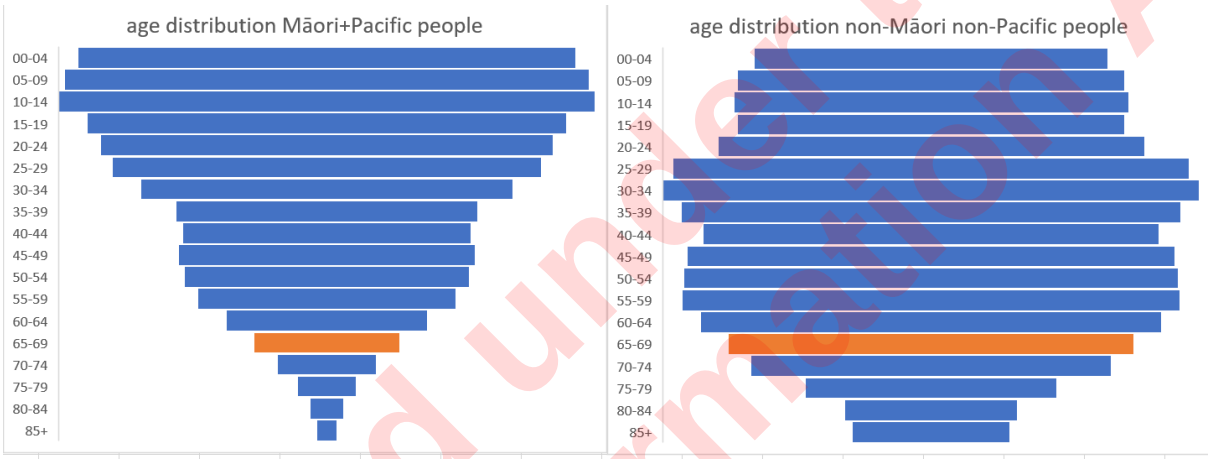
Māori and Pacific communities could therefore be particularly at risk of developing and impacted by HZ, due to a disproportionate burden of COVID-19 illness borne by these population groups.

In addition, people with diabetes mellitus and COPD have an increased risk of complications from HZ, and Māori and Pacific peoples, have a higher incidence of these comorbidities

compared to non-Māori and non-Pacific people in New Zealand. However, Pharmac staff also note that as there is limited data on HZ related hospitalisations for Māori and Pacific people, and thus the true burden from severe HZ infection in these populations is unknown.

When the Immunisation Subcommittee reviewed the cost utility of zoster vaccination at various ages at its February 2015 meeting, the subcommittee noted the need for further analysis and research to help "ensure that Māori and Pacific Island patients receive equal benefits from funded Zoster vaccination at age 65, considering their age of death is less than the rest of the population". Pharmac staff note:

- Māori and Pacific peoples' populations have younger age groups distributions than the total population, which means greater proportions dying before and smaller proportions reaching 65 years of age in order to benefit from herpes zoster vaccination under current access criteria.




- In addition, reflecting their lower life expectancies overall, the life expectancies for Māori and Pacific peoples aged 65 years are 3.3 to 4 years less than non-Māori and non-Pacific people of the same age (Statistics NZ 2021 period life tables 2017-9).[1] This means Māori and Pacific recipients of herpes zoster vaccine would gain less benefit because likelier to die earlier of general causes, thus not gaining full duration of vaccine protection compared with non-Māori non-Pacific peoples.
- Older Māori and Pacific peoples have relatively more age-related comorbid conditions predisposing to immune compromise and thus potentially lessened vaccine efficacy. This might be mitigated by vaccination at younger ages.

A NZ study on the burden of HZ cases on primary care reported a slightly lower incidence of HZ in Māori compared to other ethnicities. Factors such as VZV primary exposure in childhood and socioeconomic factors did not appear to be linked to this lower incidence (Turner et al. BMJ Open. 2018;8:e021241).

[1] where Māori males aged 65 years have a 15.8 year latest (2017-19 cohort) remaining life expectancy (rLE), vs. 19.6 years non-Māori (nM) males of the same age, a 3.8 year gap, with 16.2 years rLE for Pacific males that age; Māori females aged 65 years 17.5 years rLE vs. 21.7 years in nM, a 4.2 year gap, 18.5 years rLE in Pacific females that age; overall life expectancy of Māori males at birth 73.4 years, nM 80.9, a 7.3 year gap, Pacific males 75.4; Māori females 77.1, nM 84.4, a 7.3 year gap, Pacific females 79.0; source: New Zealand period life tables: 2017–2019 spreadsheet; where nM life expectancy understates true disparities between Māori or Pacific peoples vs. non Māori non Pacific peoples, by nM including Pacific dilutionally)

**The impact on the health outcomes of population groups experiencing health disparities**

Pharmac staff note that the younger population age distribution of Māori and Pacific peoples, combined with higher socioeconomic deprivation rates, may result in health disparities for these groups.

**The impact on Government health priorities**

Immunisation against HZ does not specifically fall into the overarching Government health priorities, however both treatments for and immunisation to prevent infectious diseases are considered priorities.

## Health Benefit

**Details of the pharmaceutical under consideration**

*Clinical Pharmacology and Mechanism of Action*

Shingrix is an adjuvanted subunit vaccine that contains recombinant VZV glycoprotein E (gE) administered via injection. By combining the VZV specific antigen (gE) with an adjuvant system (AS01B), Shingrix induces antigen-specific cellular and humoral immune responses in individuals with pre-existing immunity against VZV.

*New Zealand Regulatory Approval*

Shingrix is Medsafe approved for the prevention of herpes zoster and post-herpetic neuralgia in adults 50 years of age or older.

*Recommended Dosage*

50mcg gE antigen/0.5mL, administered as an intramuscular injection.

Schedule: primary series of two doses of 0.5mL each, administered 2-6 months apart.

*Proposed Treatment Paradigm*

Shingrix would replace the currently available live zoster vaccine for those aged 65 years and over. The Supplier has suggested that the doses can be given alongside Tdap or influenza vaccinations to limit pharmacy visits and cost. Pharmac staff note that there was some hesitation from primary care practitioners to providing an additional vaccination without an additional immunisation claim.

*Proposed Special Authority Criteria*

Shingrix is proposed for use in those aged 65 years.

*International Recommendations*

**Table 2:** International recommendations regarding the funding of Shingrix for the prevention of HZ in those aged 65 years and over

| Country (HTA Agency) | Date | Outcome | Reason |
|---|---|---|---|
| Australia (PBAC) | November 2018 | ✗ The PBAC did not recommend the listing of the varicella zoster virus vaccine (HZ/su) on the National Immunisation Program (NIP) for the prevention of herpes zoster in adults aged 60 years, with a five-year catch-up program | The PBAC considered that there was some uncertainty in the magnitude of the clinical benefit, that the incremental cost-effectiveness ratios (ICER) were highly uncertain and that the estimated financial impact was high and uncertain. Given the large opportunity cost, the PBAC considered more conservative cost-effectiveness analyses were required.<br><br>The PBAC noted the submission proposed no vaccine as the comparator for individuals aged 60-69 years and 80+ years, and the live-HZ vaccine for individuals aged 70-79 years. The comparisons presented in the submission did not enable the PBAC to consider the most appropriate age for HZ/su vaccination. |
| Canada (CADTH - CDEC) | Pharmac staff did not find any evidence of CADTH review of Shingrix in the requested, or other indications. | | |
| Scotland (SMC) | Pharmac staff did not find any evidence of SMC review of Shingrix in the requested, or other indications. | | |
| England/ Wales (NICE) | Pharmac staff did not find any evidence of NICE review of Shingrix in the requested, or other indications. | | |

The supplier has indicated that Shingrix has been licensed in 39 countries including the US, Canada, Japan, China, Brazil, Switzerland, South Korea, Singapore, Australia and the UK, and also in Europe (under a centralised procedure).

The indication to include vaccination in adults aged 18 years and older who are or will be at increased risk of HZ due to immunodeficiency or immunosuppression caused by known disease or therapy is currently registered with FDA, EMA and TGA.

## The health benefits to the person, family, whānau and wider society

*Evidence Summary*

The supplier has identified two trials (Zoe-50 and Zoe-70) that provide the primary evidence for the health benefits of the recombinant herpes zoster vaccine for those aged 65 years and older. A summary of these trials is provided in the table below (Table 3). The full text publications are available in Appendix 1.

**Table 3**: Summary of **key** evidence for the recombinant herpes zoster vaccine for those aged 65 years and over

| Trial | Study Design | Patients Group(s) | No. Patients | Intervention | Duration | Efficacy & Safety | Citation |
|---|---|---|---|---|---|---|---|
| Zoe-50 | Randomised, placebo-controlled, observer-blind, multinational, phase III trial | Adults 50 years and over | N = 15,411 | Varicella–zoster virus glycoprotein E and the AS01B adjuvant vaccine (called HZ/su; (n=7698)<br><br>Placebo (n=7713) | mean follow-up of 3.2 years | Most participants received two doses of the study vaccines (95.6% of HZ/su recipients and 96.4% of placebo recipients).<br><br>8926 participants were assigned to the reactogenicity subgroup (4460 in the HZ/su group and 4466 in the placebo group).<br><br>14,759 (95.8%) were included in the modified vaccinated cohort.<br><br>408 participants reported suspected herpes zoster. 244 (59.8%) were confirmed.<br><br>**Efficacy**<br><br>Of the 216 confirmed cases in the modified vaccinated cohort, 6 occurred in the HZ/su group and 210 in the placebo group after a mean follow-up of 3.2 years.<br><br>**Overall incidence of herpes zoster per 1000 person-years (modified cohort):**<br><br>• 0.3 in the HZ/su group<br>• 9.1 in the placebo group<br>• Overall vaccine efficacy of 97.2% (95% CI 93.7 to 99.0; P<0.001).<br><br>No significant difference in vaccine efficacy among age groups.<br><br>**Overall vaccine efficacy (total cohort):** 96.2% (95% CI 92.7 to 98.3; P<0.001)<br><br>**Safety**<br><br>Reactogenicity subgroup - symptoms within 7 days after vaccination:<br><br>• 84.4% of participants in the HZ/su group<br>• 37.8% in the placebo group<br><br>17.0% of HZ/su recipients and 3.2% of placebo recipients reported symptoms that prevented normal everyday activities (grade 3):<br><br>• Injection-site reactions (81.5% of HZ/su recipients (grade 3 in 9.5%) and 11.9% of placebo recipients (grade 3 in 0.4%))<br>  ○ Pain was the most common injection-site reaction and was reported in 79.1% of HZ/su recipients and 11.2% of placebo recipients.<br>• systemic reactions (66.1% of HZ/su recipients (grade 3 in 11.4%) and 29.5% of placebo recipients (grade 3 in 2.4%)). | Lal et al. N Engl J Med. 2015;372:2087-96 |

| Trial | Study Design | Patients Group(s) | No. Patients | Intervention | Duration | Efficacy & Safety | Citation |
|---|---|---|---|---|---|---|---|
| | | | | | | ○ Myalgia was the most common systemic reaction and was reported in 46.3% of HZ/su recipients and 12.1% of placebo recipients.<br><br>Median duration of most reaction – 1-3 days.<br><br>Grade 3 solicited systemic reactions were more frequent after the second dose (8.5%; 95% CI 7.7 to 9.4) than after the first dose (5.9%; 95% CI 5.2 to 6.6).<br><br>Within the first 30 days after vaccination, 231 serious adverse events (103 in HZ/su recipients and 128 in placebo recipients) were reported in 87 of 7698 HZ/su recipients (1.1%) and 97 of 7713 placebo recipients (1.3%) in the total vaccinated cohort.<br><br>• 4 participants (1 HZ/su recipient and 3 placebo recipients) had a serious adverse event that was considered to be related to vaccination by the investigators: hypotension with syncope, mononeuritis, neuro-sensory deafness, and musculoskeletal chest pain. | |
| Zoe-70 | Randomised, placebo-controlled, observer-blind, multinational, phase III trial | adults 70 years of age or older | N = 13,900 | Two doses of HZ/su (n= 6950)<br><br>Placebo (n= 6950) | Mean follow-up of 3.7 years | 94.4% of HZ/su recipients and 95.6% of placebo recipients received two doses.<br><br>In the pooled analysis of participants from ZOE-70 and ZOE-50, 17,531 participants 70 years of age or older were included in the total vaccinated cohort, and 16,596 were included in the modified vaccinated cohort.<br><br>Overall, 3066 participants (22.1%) were 80 years of age or older, and 76 (0.5%) were 90 years of age or older.<br><br>432 suspected episodes of herpes zoster were reported, 270 of which were confirmed as herpes zoster; 246 occurred in the modified vaccinated cohort: 23 in HZ/su recipients and 223 in placebo recipients.<br><br>**Efficacy**<br><br>The incidence of herpes zoster per 1000 person-years was 0.9 in the HZ/su group and 9.2 in the placebo group, for an overall vaccine efficacy of 89.8% (95% CI 84.2 to 93.7; P<0.001).<br><br>Vaccine efficacy did not differ significantly between the two age groups (90.0% among participants 70 to 79 years of age and 89.1% among participants ≥80 years of age).<br><br>Pooled analysis of Zoe-50 and Zoe-70 participants aged 70 years or older<br><br>• 25 confirmed cases of herpes zoster occurred in HZ/su recipients<br>• 284 cases in placebo recipients<br>• vaccine efficacy of 91.3% against herpes zoster (95% CI 86.8 to 94.5%) | Cunningham et al. N Engl J Med. 2016;375:1019-32 |

| Trial | Study Design | Patients Group(s) | No. Patients | Intervention | Duration | Efficacy & Safety | Citation |
|---|---|---|---|---|---|---|---|
| | | | | | | Vaccine efficacy did not differ significantly between the two age groups (91.3% in participants 70 to 79 years of age and 91.4% in participants ≥80 years of age).<br><br>Vaccine efficacy was 97.6% during year 1, 92.0% during year 2, 84.7% during year 3, and 87.9% during year 4 after the second vaccination.<br><br>**Vaccine efficacy against PHN**<br><br>In the pooled modified vaccinated cohort that included all participants 50 years of age or older, PHN developed in 4 of 32 HZ/su recipients and in 46 of 477 placebo recipients with herpes zoster.<br><br>The incidence of postherpetic neuralgia per 1000 person-years was 0.1 in the HZ/su group and 0.9 in the placebo group, for a vaccine efficacy of 91.2% among adults 50 years of age or older (95% CI 75.9 to 97.7%; P<0.001).<br><br>Postherpetic neuralgia did not develop in any HZ/su recipients younger than 70 years of age.<br><br>Among participants 70 years of age or older, vaccine efficacy against postherpetic neuralgia was 88.8% (95% CI, 68.7 to 97.1%; P<0.001).<br><br>**Safety**<br><br>1025 participants (7.4%) were randomly assigned to the reactogenicity subgroup (512 HZ/su recipients and 513 placebo recipients).<br><br>Reactions - 79.0% of HZ/su recipients and in 29.5% of placebo recipients.<br><br>Injection-site reactions:<br><br>• 74.1% of HZ/su recipients<br>• 9.9% of placebo recipients.<br>  ○ Grade 3 injection-site reactions were reported in 8.5% of HZ/su recipients and in 0.2% of placebo recipients.<br><br>Systemic reactions:<br><br>• 53.0% of HZ/su recipients<br>• 25.1% of placebo recipients<br>  ○ grade 3 reactions were reported in 6.0% and 2.0%, respectively).<br><br>In the HZ/su group, the most common injection-site reaction was pain (in 68.7% of HZ/su recipients) and the most common systemic reaction was fatigue (in 32.9%). Median duration of reaction 1-3 days. | |

| Trial | Study Design | Patients Group(s) | No. Patients | Intervention | Duration | Efficacy & Safety | Citation |
|---|---|---|---|---|---|---|---|
| | | | | | | The overall frequency and severity of the solicited reactions did not increase significantly after the second dose.<br><br>Serious adverse events occurred in 16.6% of HZ/su recipients and in 17.5% of placebo recipients, and potential immune-mediated diseases occurred in 1.3% of HZ/su recipients and in 1.4% of placebo recipients.<br><br>12 HZ/su recipients (0.2%) and in 8 placebo recipients (0.1%) were considered to have serious adverse events related directly to the trial intervention.<br><br>426 participants in the HZ/su group (6.1%) and 459 participants in the placebo group (6.6%) died. One was considered to be due to the HZ/su vaccine (participant with preexisting thrombocytopenia had acute myeloid leukemia diagnosed 75 days after the first dose of HZ/su). | |
| Interim result from extension study of Zoe-50 and -70 | Ongoing open-label, phase 3B, long-term follow-up study | Zoe-50/70 participants | Of the 14 648 ZOE-50/70 participants who received at least 1 RZV dose, 7413 (50.6%) were enrolled for the long-term efficacy assessment | Recombinant zoster vaccine (RZV)<br><br>Placebo | ≥2 additional years of follow-up (between 5.1 and 7.1 years [mean] post vaccination) | 7277 had previously received both RZV doses and were included in the modified total vaccinated cohort (mTVC) for the efficacy assessments, 813 in the according-to-protocol (ATP) cohort for humoral immunity persistence, and 108 in the ATP cohort for cell-mediated immune (CMI) persistence.<br><br>**Efficacy**<br><br>27 and 169 confirmed HZ cases occurred in the vaccine and control groups, respectively. RZV was 84.0% (95% CI 75.9–89.8) efficacious in preventing HZ (ranging from a mean of approximately 5.1 to approximately 7.1 years post-vaccination).<br><br>Through the entire post-vaccination follow-up period, ranging from 1-month post-dose 2 to a mean of approximately 7.1 years post-vaccination, 59 and 651 confirmed HZ cases occurred in the vaccine and control groups, respectively, and thus efficacy of RZV against HZ was 90.9% (95% CI 88.2–93.2).<br><br>Annual vaccine efficacy estimates reached a plateau >84% between Y4 and Y6 post-vaccination.<br><br>**Safety**<br><br>No deaths or other SAEs were considered causally related to vaccination. | Boutry et al. Clin infect Dis. 2021; ciab629 |
| Effectiveness of the Recombinant Zoster Vaccine | Retrospective cohort study | Non-immunocompromised, vaccine age– | N=4,769,819 | Recombinant zoster vaccine (RZV) | Median duration of follow-up was 7.0 months | 298 cases of HZ with a total follow-up time of 115 125 person-years in the vaccinated cohort.<br><br>64 169 HZ cases with a total follow-up time of 7 184 911 person-years in the unvaccinated cohort.<br><br>The incidence rate of HZ was 258.8 (95% CI 230.6–289.4) cases per 100 000 person-years in vaccinated individuals compared with 893.1 (95% CI 886.2–900.0) cases per 100 000 person-years in the unvaccinated individuals. | Sun et al. Clin Infect Dis. 2021;73:949-56 |

| Trial | Study Design | Patients Group(s) | No. Patients | Intervention | Duration | Efficacy & Safety | Citation |
|---|---|---|---|---|---|---|---|
| in Adults Aged 50 and Older in the United States | | eligible individuals | | Compared to unvaccinated individuals | after vaccination | Overall adjusted vaccine effectiveness was 85.5% (95% CI 83.5–87.3%), with an effectiveness of 86.8% (95% CI, 84.6–88.7%) in individuals aged 50 to 79 years old compared with 80.2% (95% CI, 75.1–84.3%) in individuals aged 80 and older.<br><br>In the sensitivity analysis requiring 5 years of continuous enrollment prior to the index date, a total of 1 569 520 individuals with 2 039 740 person-years were included. The overall RZV effectiveness was 86.7% (95% CI 83.3–89.4%).<br><br>In those with a history of zoster vaccine live (ZVL) within 5 years prior, the incidence rate of HZ was 239.4 (95% CI, 142.8–371.8) cases per 100 000 person-years in individuals vaccinated with RZV and 754.5 (95% CI, 718.4–791.7) cases per 100 000 person-years in unvaccinated individuals.<br><br>In individuals with no history of ZVL within 5 years prior to the index date, the incidence rate of HZ was 260.9 (95% CI, 205.9–325.0) cases per 100 000 person-years in individuals vaccinated with RZV and 908.1 (95% CI, 895.0–921.3) cases per 100 000 person-years in unvaccinated individuals.<br><br>In the cohort with no history of ZVL, unadjusted vaccine effectiveness was 76.1% (95% CI, 70.0–81.0%) and adjusted effectiveness was 87.1% (95% CI, 83.4–89.9%).<br><br>In adults with a history of ZVL within 5 years prior to the index date, unadjusted vaccine effectiveness was 71.2% (95% CI, 53.4–82.2%) and adjusted effectiveness was 84.8% (95% CI, 75.3–90.7%). | |
| Effectiveness of the recombinant zoster vaccine among Kaiser Permanente Hawaii enrollees aged 50 and older | Retrospective cohort study | Immunocompetent, vaccine age-eligible individuals without a prior history of HZ | N= 78,356 | RZV vaccine | Median follow-up time was 730 days | 11 864 (15.1%) adults received two valid doses of the recombinant zoster vaccine.<br><br>27 HZ cases were reported among patients who were fully vaccinated during a total of 8 291 vaccinated person-years.<br><br>The incidence rate of HZ during vaccinated person-time was 325.6 cases per 100 000 person-years (95% CI 217.7-464.4).<br><br>Total of 1 273 HZ cases occurred with 119 719 person-years of unvaccinated person-time.<br><br>The incidence rate of HZ during unvaccinated person-time was 1063.3 HZ cases per 100 000 person-years (95% CI 1006-1122.8).<br><br>The incidence rate of HZO for vaccinated person-time was 11.9 cases per 100 000 person-years (95% CI 0.7-52.3).<br><br>The incidence rate of HZO for unvaccinated person-time was 72.1 cases per 100 000 person-years (95% CI 58.0-88.3). | Sun et al. Vaccine. 2021;39:3974-82 |

| Trial | Study Design | Patients Group(s) | No. Patients | Intervention | Duration | Efficacy & Safety | Citation |
|---|---|---|---|---|---|---|---|
| | | | | | | Overall adjusted vaccine effectiveness in preventing HZ was 83.5% (95% CI 74.9-89.2), with an effectiveness of 67.7% (95% CI 11.8-88.1) for individuals aged 60 to 69, 83.8% (95% CI 70.1-90.7) for individuals aged 70 to 79, and 86.4% (95% CI 73.5-93.0) for individuals aged 80 and above.<br><br>The overall adjusted vaccine effectiveness in preventing HZOwas 93.3% (95% CI 48.7-99.1). | |
| Effectiveness of the Recombinant Zoster Vaccine for Herpes Zoster Ophthalmicus | Retrospective, observational cohort study (United States) | Those who were age eligible for herpes zoster (HZ) vaccination (50 years of age or more) | N = 4,84,579 | RZV vaccination | Median follow-up 730 days | 3.7% received a valid 2-dose regimen of RZV.<br><br>The incidence rate of HZO was 25.5 cases (95% CI 17.4-35.8 cases) per 100 000 person-years in the vaccinated group, whereas the rate was 76.7 cases (95% CI 74.7-78.7 cases) per 100 000 person-years in the unvaccinated group.<br><br>The overall adjusted effectiveness of RZV was 89.1% (95% CI 82.9%-93.0%).<br><br>Adjusted RZV effectiveness was 87.6% (95% CI 59.9%-96.2%) for those 60 to 69 years of age and 88.9% (95% CI 80.6%-93.7%) for those 70 to 79 years of age. Adjusted RZV effectiveness was 88.8% (95% CI 77.5%-94.5%) for those 80 years of age or older. | Lu et al. Ophthalmology. 2021;128:1299-707 |
| Shingrix: Real-World Effectiveness in the First 2 Years Post-Licensure | Prospective cohort study | Beneficiaries aged >65 years | N=15,589,546 beneficiaries | RZV vaccine | | There were 2152 HZ cases in the 1-dose cohort (478 532 person-years) and 1880 HZ cases in the 2-dose cohort (608 928 person-years). 258 293 met the HZ case definition while in the unvaccinated cohort.<br><br>For every 1000 person-years, there were 10.32 HZ cases among unvaccinated beneficiaries, while there were 4.50 HZ and 3.09 HZ cases among 1-dose and 2-dose vaccinees, respectively.<br><br>2-dose VE in preventing community HZ = 70.1% (95% CI 68.6–71.5)<br><br>1-dose VE in preventing community HZ = 56.9% (95% CI 55.0–58.8)<br><br>The 2-dose VE among immunocompromised beneficiaries was 64.1% (95% CI, 57.2–69.8), while among immunocompetent beneficiaries it was 70.9% (95% CI, 69.3–72.4).<br><br>• HR 1.22 (95% CI 1.02–1.46)<br><br>Among individuals who had received a ZVL vaccination during the 5 years prior to RZV, the 2-dose and 1-dose VE were 63.0% (95% CI 58.3–67.2) and 51.0% (95% CI 45.4–56.0), respectively.<br><br>Having received a prior ZVL vaccination resulted in a HZ incidence of 8.5 (95% CI 8.4–8.6) per 1000 person-years in the RZV unvaccinated cohort compared with an outcome rate of 10.6 (95% CI 10.6– | Izurieta et al. Clin Infect Dis. 2021;73:941-8 |

| Trial | Study Design | Patients Group(s) | No. Patients | Intervention | Duration | Efficacy & Safety | Citation |
|---|---|---|---|---|---|---|---|
| | | | | | | 10.6) per 1000 person-years in the RZV unvaccinated cohort who did not receive ZVL in the prior 5 years.<br><br>ophthalmic zoster: 2-dose VE of 66.8% (95% CI 60.7–72.0) and a 1-dose VE of 44.7% (95% CI 36.0–52.3)<br><br>PHN secondary analysis reported a 2-dose VE of 76.0% (95% CI 68.4–81.8) and a 1-dose VE of 51.4% (95% CI 42.0–59.2). | |

The supplier also provided or referenced the following studies in support of their application:

- McGirr et al. Vaccine. 2019;37:2896-909: an indirect comparison network meta-analysis undertaken by GSK staff comparing the relative efficacy and safety of vaccines for prevention of herpes zoster (HZ); adjuvanted recombinant zoster vaccine (RZV) and zoster vaccine live (ZVL). RZV reported significantly higher HZ efficacy than ZVL in adults 60 years of age or older (VE RZV = 0.92 (95% CI 0.88, 0.94), VE ZVL = 0.51 (95% CI 0.44, 0.57)) and adults 70 years or older (VE RZV = 0.91 (95% CI 0.87, 0.94), VE ZVL = 0.37 (95% CI 0.25, 0.48)). Similarly, RZV reported significantly higher PHN efficacy than ZVL in adults 60 years or older (VE RZV = 0.89 (95% CI 0.70, 0.96), VE ZVL = 0.66 (95% CI 0.48, 0.78)) and adults 70 years or older (VE RZV = 0.89 (95% CI 0.69, 0.96), VE ZVL = 0.67 (95% CI 0.44, 0.80)).

  There were no statistically significant differences reported between RZV and any formulation of ZVL or placebo for SAEs.

  Pharmac staff note that this is a low-grade study, and that it was conducted by GSK employees, and funded by the supplier.

- Godeaux et al. Hum Vaccin Immunother. 2017;13:1051-8: a phase III, non-randomised, open-label, multi-centre study evaluating the immunogenicity and safety of an adjuvanted recombinant subunit herpes zoster (HZ) vaccine (HZ/su) in adults aged 50 years or older with prior physician-documented history of HZ. Participants (stratified by age: 50–59, 60–69 and 70 years or older) received 2 doses of HZ/su 2 months apart and were followed-up for another 12 months.

  The vaccine response rate (VRR) for anti-gE antibodies at month 3 (1 month after the second vaccine dose) was 90.2% (95% CI 81.7–95.7). The median fold increase in anti-gE antibody concentrations from pre-vaccination to Month 3 was 25.6 (first and third quartiles [Q1, Q3]: 10.2, 43.8). Results were comparable for all age-groups.

  Overall, 77.9% (95% CI 68.2–85.8) of participants reported at least 1 local solicited AE and 71.6% (95% CI 61.4–80.4) of participants reported at least 1 general solicited AE.

- Hastie et al. J Infect Dis. 2021;224:2025-34: a single-arm, open-label, phase IIIB, long-term follow-up study investigating the immunogenicity of the adjuvanted recombinant zoster vaccine: persistence and anamnestic response to additional doses administered 10 years after primary vaccination (N=70). Humoral and cell-mediated immune (CMI) responses to 2 initial RZV doses were assessed.

  Ten years after initial vaccination, humoral and CMI responses were approximately 6-fold and 3.5-fold, respectively, above those before the initial vaccination levels. Predicted immune persistence through 20 years after initial vaccination was similar across the 3 models. Sixty-two participants (mean age [standard deviation], 82.6 [4.4] years) received ≥1 additional RZV dose. Strong anamnestic humoral and CMI responses were elicited by 1 additional dose, without further increases after a second additional dose.

- Ocran-Appiah et al. Vaccine. 2021;39:6-10: a phase IIIB, non-randomized, open-label, multinational safety study of adults aged 50 years or older who received placebo in the

Zoe-50 and Zoe-70 trials, who subsequently were invited to receive two intramuscular doses of RZV, 2 months apart. Those who had confirmed HZ during the Zoe trial periods were eligible. 8687 participants were enrolled in this study and received RZV; 97.8% completed the 2-dose vaccination schedule.

During the 30-day post-vaccination period, at least one unsolicited AE was reported by 5175 (59.6%) participants, 4422 (50.9%) of them experienced AEs related to vaccination as assessed by the investigator. Unsolicited AEs of grade 3 intensity were reported by 963 (11.1%) participants; 640 (7.4%) of those experienced an AE considered causally related to vaccination. Across the different age strata, at least one unsolicited AE was reported by 71.3% (50–59 years), 67.5% (60–69 years), 57.9% (70–79 years), and 48.3% (80 years or older) of participants.

The most common SAEs were pneumonia, reported by 54 participants (0.6% [95%CI: 0.5–0.8]), cardiac failure (28 participants; 0.3% [95%CI: 0.2–0.5]), atrial fibrillation (25 participants; 0.3% [95%CI: 0.2–0.4]), myocardial infarction (18 participants; 0.2% [95%CI: 0.1–0.3]), and acute myocardial infarction (18 participants; 0.2% [95%CI: 0.1–0.3]).

**Literature Search**

Pharmac staff conducted a PubMed search on **12/04/2022** (search terms: recombinant zoster vaccine) and identified two additional publications regarding recombinant zoster vaccine for HZ that were not identified by the supplier (Appendix 2).

- Curran et al. J Am Geriatr Soc. 2021;69:744-52: data from the Zoe-50 and Zoe-70 studies were pooled to investigate the effect of RZV on frail individuals. 45.6% were considered pre-frail and 11.3% frail, based on the frailty index used in the Zoe trials. RZV vaccine efficacy against herpes zoster was >90% for all frailty subgroups (non-frail: 95.8% (95% CI 91.6-98.2), pre-frail: 90.4% (84.4-94.4), frail: 90.2% (75.4-97.0)). The percentage of participants reporting solicited adverse events tended to decrease with increasing frailty.

- Curran et al. J Gerontol A Biol Sci Med Sci. 2019;74:1231-38: as assessment of the efficacy of an adjuvanted recombinant zoster vaccine in reducing the HZ burden of illness, HZ burden of interference with activities of daily living, and HZ impact on quality of life using data from ZOE-50 and ZOE-70.

  The estimated vaccine efficacy in reducing HZ burden of illness and HZ burden of interference was greater than 90% in both the ZOE-50 and the pooled ZOE-70 analysis. In confirmed HZ cases, adjuvanted recombinant zoster vaccine reduced the maximal Zoster Brief Pain Inventory (ZBPI) worst-pain score in the pooled ZOE-70 analysis (p = .032) and the maximal ZBPI average-pain scores in both the ZOE-50 (p = .049) and the pooled ZOE-70 analysis (p = .043). In breakthrough HZ cases, trends for diminished loss of quality of life compared with placebo-recipient HZ cases were observed, with differences up to 0.14 on the EQ-5D index at time points during the four weeks following HZ onset.

**Consequences for the health system**

Detailed screening prior to vaccination as is currently required for the live zoster vaccine in New Zealand is not required with Shingrix.

Shingrix is administered as a two dose primary series vaccine, which means that protocols would need to be implemented to ensure a second dose can be administered (2-6 months after the first dose). The supplier has suggested that administration alongside other vaccines for the requested age group would mitigate the need for additional appointments and healthcare resource.

## Suitability

**The features of the medicine or medical device that impact on use**

Shingrix has a longer shelf-life than the currently available vaccine; three years, compared to the 18 months.

Reconstituted vaccine should be used promptly but may be stored up to six hours at 2-8 degrees Celsius, if required.

SHINGRIX is supplied as two vials, one containing a single dose of gE (active ingredient) in a lyophilised form which needs to be reconstituted using the other vial containing a single dose of the Adjuvant System AS01B in suspension.

## Costs and Savings

**PICO (Population, Intervention, Comparator, Outcome)**

Table **4** below summarises Pharmac staff's interpretation of the PICO for vaccination with recombinant zoster vaccine if it were to be funded in New Zealand for people aged 65 years and over.

This PICO captures key clinical contexts, helping review the proposal and frame any future economic assessment by Pharmac. We seek the Committee's advice on the content in the table below.

Note that the PICO may change as clinical and other features evolve.

**Table 4:** PICO for [**the pharmaceutical**] if it were to be funded in New Zealand for [**the indication**].

| | |
|---|---|
| **P**opulation | Patients aged 65 years of age with a two-year catch-up programme for those aged 66 and over. |
| **I**ntervention | two doses of recombinant varicella zoster virus glycoprotein E (SHINGRIX) spaced 2-6 months apart<br>+ BSC (acyclovir or valaciclovir+ capsaicin cream) |
| **C**omparator(s) (NZ context) | No vaccination + BSC (acyclovir tablets + capsaicin cream) |
| **O**utcome(s) | Reduced incidence of herpes zoster episodes<br>Reduced postherpetic neuralgia<br>Health sector savings from reduced inpatient and outpatient events<br>Improved health related quality of life |
| *Table definitions:*<br>**P**opulation: The target population for the pharmaceutical, including any population defining characteristics (eg. line of therapy, disease subgroup)<br>**I**ntervention: Details of the intervention pharmaceutical (dose, frequency, treatment duration/conditions for treatment cessation).<br>**C**omparator: Details the therapy(s) that the patient population would receive currently (status quo – including best supportive care; dose, frequency, treatment duration/conditions for treatment cessation).<br>**O**utcomes: Details the key therapeutic outcome(s), including therapeutic intent, outcome definitions, timeframes to achieve outcome(s), and source of outcome data. | |

### Costs and savings to pharmaceutical expenditure

Costs and savings are not addressed in this paper as the supplier has not yet submitted a commercial proposal for this vaccine. In this paper, Pharmac staff are seeking the Committee's advice on factors such as dosing and catch-up programmes, which would inform the subsequent assessment of a later commercial proposal.

## APPENDICES

**Appendix 1:**

Lal et al. N Engl J Med. 2015;372:2087-96

Cunningham et al. N Engl J Med. 2016;375:1019-32

Boutry et al. Clin infect Dis. 2021; ciab629

Sun et al. Clin Infect Dis. 2021;73:949-56

Sun et al. Vaccine. 2021;39:3974-82

Lu et al. Ophthalmology. 2021;128:1299-707

Izurieta et al. Clin Infect Dis. 2021;73:941-8

McGirr et al. Vaccine. 2019;37:2896-909

Godeaux et al. Hum Vaccin Immunother. 2017;13:1051-8

Hastie et al. J Infect Dis. 2021;224:2025-34

Ocran-Appiah et al. Vaccine. 2021;39:6-10

**Appendix 2:**

Curran et al. J Am Geriatr Soc. 2021;69:744-52

Curran et al. J Gerontol A Biol Sci Med Sci. 2019;74:1231-38

## THE FACTORS FOR CONSIDERATION

Factors are presented here in the order they appear in the paper, without implying any ranking or relative importance.

### NEED

- The health need of the person
- The availability and suitability of existing medicines, medical devices and treatments
- The health need of family, whānau, and wider society
- The impact on the Māori health areas of focus and Māori health outcomes
- The impact on the health outcomes of population groups experiencing health disparities
- The impact on Government health priorities

### HEALTH BENEFITS

- The health benefit to the person
- The health benefit to family, whānau and wider society
- Consequences for the health system

### SUITABILITY

- The features of the medicine or medical device that impact on use by the person
- The features of the medicine or medical device that impact on use by family, whānau and wider society
- The features of the medicine or medical device that impact on use by the health workforce

### COSTS AND SAVINGS

- Health-related costs and savings to the person
- Health-related costs and savings to the family, whānau and wider society
- Costs and savings to pharmaceutical expenditure
- Costs and savings to the rest of the health system