6.07 Recombinant Zoster Vaccine, Powder and suspension for injection (0.5mL) Shingrix®, GSK Australia Pty Ltd.

1 Purpose of submission

1.1 The Category 2 submission requested National Immunisation Program (NIP) listing for recombinant zoster vaccine (RZV) with age eligibility criteria for non-Indigenous adults reduced from individuals aged 65 years of age (YOA) and over to individuals aged 60 YOA and over for prevention of herpes zoster (HZ) and post-herpetic neuralgia (PHN).

1.2 Listing was requested on the basis of a cost-effectiveness analysis versus vaccination at ≥65 years.

Table 1: Key components of the clinical issue addressed by the submission (as stated in the submission)

Component	Description
Population	Non-Indigenous adults 60-64 y
Intervention	RZV: 2 doses administered 2-6 months apart.
Comparator	No vaccination from 60-64 y to inform economic comparison of delayed vaccination with RZV at 65 y (i.e., no vaccination from 60-64 YOA, followed by RZV at 65 YOA).
Outcomes	Efficacy: VE vs HZ; VE vs PHN; VE vs non-PHN HZ-related complications Safety: Solicited local and general AEs during the 7 days post vaccination; Unsolicited AEs during the 30 days post vaccination; All SAEs up until end of LTFU in ZOSTER-049
Clinical claim	In non-Indigenous adults vaccinated at 60-64 y, RZV has superior efficacy and 'slightly' inferior safety when compared to no vaccination from 60-64 y. Overall, safety is comparable when vaccinated at 60-64 y compared to delayed vaccination at 65 y.

Source: Table 1-1: Key components of the clinical issue addressed by the submission, p25 of the submission.
AE = adverse event; HZ = herpes zoster (shingles), LTFU = long term follow-up; PHN = post-herpetic neuralgia; RZV = recombinant zoster vaccine; SAE = serious adverse event; VE =vaccine efficacy, y = year(s).

2 Background

Registration status

2.1 RZV was TGA registered on 2 July 2018 for the prevention of HZ and PHN in adults aged ≥50 years and extended to include adults aged ≥18 years at increased risk of HZ on 16 December 2021.

Previous PBAC consideration

2.2 At its March 2023 meeting, the PBAC recommended the inclusion of RZV on the NIP for the prevention of HZ and PHN for non-Indigenous individuals aged 70 years, Aboriginal and Torres Strait Islander individuals aged ≥50 years and immunocompromised individuals aged ≥18 years with specified medical conditions at high risk of HZ infection. The PBAC recommended expanding the list of specified

medical conditions at its November 2023 meeting to include several additional conditions and immunosuppressive therapies which the Australian Technical Advisory Group on Immunisation (ATAGI) considered conferred a moderate or high risk for HZ.

2.3 At its March 2023 meeting, the PBAC did not recommend RZV for non-Indigenous individuals aged 65 to 69 years and aged ≥71 years. At its July 2023 meeting, the PBAC recommended that RZV be a designated vaccine for the purposes of the *National Health Act 1953*, for individuals aged 65 YOA (primary program) and older (catch-up program).

3 Requested listing

Vaccine and the circumstances in which vaccine may be provided	Proposed NNP	Brand	Formulation	Number and timing of doses
Recombinant varicella zoster virus glycoprotein E antigen ($AS01_B$ Adjuvanted) vaccine	$[redacted]	Shingrix	Powder and suspension for injection, 0.5 mL	a. Two primary doses 2 to 6 months apart b. For subjects who are immunodeficient, immunosuppressed or likely to become immunosuppressed due to known disease or therapy, two primary doses can be given 1 to 2 months apart
Circumstances Vaccine may be provided to a person who: (a) is at least 60 years of age; or b) is an Aboriginal and Torres Strait Islander individual who is at least 50 years of age; or (c) is at least 18 years of age and considered at increased risk of herpes zoster, due to an underlying condition and/or immunomodulatory/immunosuppressive treatments as specified.				

NNP = nationally negotiated price

3.1 The submission proposed an amendment to the current NIP listing for RZV in non-Indigenous adults aged ≥65 years, to lower the minimum age to 60 years. The listing would be otherwise unchanged.

3.2 Individuals aged 60-64 YOA who are considered at moderate to severe risk of HZ, due to an underlying immunocompromising condition and/or immunomodulatory/ immunosuppressive treatments currently qualify for RZV on the NIP.

For more detail on PBAC's view, see section 7 PBAC outcome.

4 Population and disease

4.1 Infection in humans with varicella zoster virus (VZV) causes varicella (chickenpox). After primary infection, the virus becomes latent in nerve ganglia of the head and neck. Reactivation of the latent infection in later life causes HZ, or shingles, a localised, painful, vesicular skin rash characterised by vesicles distributed along a single

dermatome. The rash is usually accompanied by acute, severe, and disabling pain typically lasting 10 – 15 days, causing interference with daily activities and scarring in many individuals. In Australia, HZ is a notifiable disease.

4.2 The Australian Immunisation Handbook (AIH) states the lifetime risk of HZ for people who live to 80 YOA is around 50% (AIH 2025[1]). Older adults are particularly susceptible, and the risk of HZ and its complications increases with age as VZV-specific immune response declines. Two-thirds of HZ cases occur in individuals ≥50 years (Kawai et al, 2014[2]; MacIntyre et al, 2015[3]; Sheel et al, 2018[4]). Based on ATAGI advice, the submission proposed an annual HZ incidence rate in the 60-64 year cohort of 1.08% (a mean of 1.26% [from MacIntyre et al, 2015, adjusted for age] and 0.89% [from Qian et al, 2022[5]]).

4.3 HZ is associated with complications that occur more often in older adults (≥50 years), with incidence and severity increasing according to age. The most common HZ-associated complication is PHN, which can be defined as chronic neuropathic pain persisting for at least three months after rash onset (AIH 2025; Stein et al, 2009[6]). An Australian study reported rates of PHN of 15% in adults 50-69 years and 26% in adults ≥80 years (MacIntyre et al, 2015). Other less common complications depend on the site of VZV reactivation and can include conditions such as keratitis, pneumonia or rarely, disseminated HZ.

4.4 The proposed lowering of the age eligibility for non-Indigenous adults to ≥60 years would bring forward doses that would otherwise be administered at 65 years. The need for a booster dose remains unknown due to uncertain waning (administration of a booster dose is not currently TGA-approved for RZV). This could increase adverse outcomes in adults over 70 YOA with worse consequences than for the same events

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1 https://immunisationhandbook.health.gov.au/contents/vaccine-preventable-diseases/zoster-herpes-zoster [last updated 7 February 2025]

2 Kawai, Gebremeskel, & Acosta. (2014). Systematic review of incidence and complications of herpes zoster: towards a global perspective. BMJ Open, 4(6), e004833–e004833. https://doi.org/10.1136/bmjopen-2014-004833.

3 MacIntyre, Stein, Harrison, Britt, Mahimbo, & Cunningham. (2015). Increasing Trends of Herpes Zoster in Australia. PLOS ONE, 10(4), e0125025. https://doi.org/10.1371/journal.pone.0125025

4 Sheel, Beard, Quinn, Dey, Kirk, Koehler, Markey, McIntyre, & Macartney. (2018). Australian vaccine preventable disease epidemiological review series: varicella-zoster virus infections, 1998–2015. Commun Dis Intell.

5 Qian, Macartney, Heywood, Sheridan, & Liu. (2021). Risk of recurrent herpes zoster in a population-based cohort study of older adults. Journal of the American Academy of Dermatology, 85(3), 611–618. https://doi.org/10.1016/j.jaad.2020.06.1013

6 Stein, Britt, Harrison, Conway, Cunningham, & MacIntyre. (2009). Herpes zoster burden of illness and health care resource utilisation in the Australian population aged 50 years and older. Vaccine. https://doi.org/10.1016/j.vaccine.2008.11.012

occurring in the target 60-64 YOA cohort due to pushing back an at-risk period after vaccination waning.

5 Comparator

5.1 The submission nominated RZV vaccination at ≥65 years as the comparator. There are no alternative vaccines for HZ. The live zoster vaccine was removed from the NIP (31 October 2023) and the Australian Register of Therapeutic Goods (December 2024).

6 Consideration of the evidence

Sponsor hearing

6.1 The sponsor requested a hearing for this item. The clinician noted protecting individuals aged 60 to 64 years of age was just as important as protecting individuals 65 to 69 years of age as the burden of HZ and PHN was similar. The clinician outlined the design and results of the ZOSTER-049 study and emphasised the strength of the evidence regarding long term protection, noting the use of historical controls likely biased against RZV as it did not account for increasing age. The clinician considered the immunogenicity data supported the robustness of the results of the ZOSTER-049 study.

Consumer inputs

6.2 The PBAC noted and welcomed the input from health care professionals (5), medical organisations (3), consumer groups (7) and individuals (2) for this item.

6.3 All health practitioner and health care professional inputs were supportive of broader subsidised access to RZV. Comments from health care professionals and medical organisations noted the increased risk of HZ infection and associated morbidity outcomes with increasing age, and the health system resource utilisation associated with managing morbidity outcomes which may be prevented where broader RZV access were available. Medical organisations also emphasised importance of RZV utilisation as preventative care and mitigating risk of HZ infection and consequential long-term patient health complications including neuropathic pain.

6.4 Comments from consumer groups and individuals also supported the expansion of the eligible population that can access subsidised RZV. Comments from Lung Foundation Australia noted the improvements in quality of life, productivity benefits (citing ABS labour force data that 64% of people aged 60-64 were active participants in the workforce) and alleviation of significant direct cost burdens for individual patients. PainAustralia and the Country Women's Association of NSW (CWANSW) noted the indirect health system and carer costs associated with HZ infection, especially where access to primary healthcare and treatment is already limited by geography and health practitioner availability, as is the case in rural and regional areas.

6.5 Consumer groups with a particular advocacy focus on clinical conditions which can present additional risk factors (Lung Foundation, Crohn's and Colitis Australia (CCA), Spleen Australia, Kidney Health Australia, Hearts4heart) noted the additional morbidity and/or mortality risks associated with HZ infections for particular subpopulations that have chronic medical conditions, including but not limited to chronic obstructive pulmonary disease , Chronic Kidney Disease and Inflammatory Bowel Disease (IBD). Spleen Australia and CCA further advocated for the immunocompromised patient definition to be expanded to ensure subsidised access to RZV for certain at-risk populations. These include asplenic patients aged 50 years and over (especially those patients who have experienced multiple episodes of shingles), or patients on (or about to commence) therapies that result in immunosuppression (such as some IBD treatments).

6.6 Input from the Immunisation Foundation of Australia (IFA) and the Australian College of Nurse Practitioners (ACNP) emphasising the clinical complications (post-herpetic neuralgia, chronic neuropathic pain, visual loss, hearing impairment and encephalitis), personal and societal burden that arise from HZ infection. Input noted that the burdens associated with HZ infection would be reduced with broader subsidised access to RZV as a health preventative measure, as well as the efficacy of RZV and health outcome benefits compared to using existing treatments for HZ infection, including legacy vaccines and antiviral medications. The PBAC also noted advice from The ACNP were supportive of expanding subsidised access for all patients aged 50 years and over (in line with the TGA-approved indication).

Clinical trials

6.7 The submission was based on:

- Two head-to-head randomised controlled trials (RCTs) comparing RZV to placebo (ZOE-50 [N=15,411] and ZOE-70 [N=13,900]). The ZOE-50/-70 trials have previously been considered by PBAC (November 2018 and March 2023) and were unchanged for this submission.
- One key single arm extension study, ZOSTER-049, which drew on vaccinated participants only from the ZOE-50/-70 trials (14,645 subjects received at least one RZV dose across both studies). The ZOSTER-049 study enrolled 7,534 (51.4%) of the ZOE-50/-70 vaccinated participants. The study commenced a median 5.6 years after the second dose of RZV in ZOE-50/-70 and was completed at a median of 11.4 years post-vaccination in ZOE-50/-70 (approximately six years trial duration). Data from interim analyses of ZOSTER-049 were previously considered in the March 2023 submission (results up to a mean 9.6 years post-vaccination).

6.8 Vaccine efficacy (VE) against HZ, PHN and non-PHN complications were presented based on the ZOSTER-049 final analysis compared to a historical control over the duration of the long-term follow up period; i.e. timing of analysis starts approximately six years post-vaccination

6.9 A follow-up study of ZOSTER-049 is currently ongoing assessing protection up to 15 years post initial vaccination, and 10 years post booster vaccination (ZOSTER-101, NCT05371080[7]).

6.10 Details of the key trials presented in the submission are provided in Table 2.

[7] Study Details | NCT05371080 | A Study on the Long-term Efficacy, Safety and Persistence of Immune Response of a Vaccine Against Herpes Zoster in Older Adults | ClinicalTrials.gov

Table 2: Key trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
ZOE-50 (NCT01165177)	CSR: Efficacy, safety, and immunogenicity study of GlaxoSmithKline (GSK) Biologicals' Herpes Zoster (HZ) vaccine GSK1437173A in adults aged ≥50 years. Primary publication: Lal H, Cunningham AL, Godeaux O, Chlibek R, Diez-Domingo J, Hwang SJ, Levin MJ, McElhaney JE, Poder A, Puig-Barberà J, Vesikari T. Efficacy of an adjuvanted herpes zoster subunit vaccine in older adults.	End of study CSR (data lock point 12 October 2015) New England Journal of Medicine. 2015 May 28;372(22):2087-96.
ZOE-70 (NCT01165229)	CSR: Efficacy, safety, and immunogenicity study of GlaxoSmithKline (GSK) Biologicals' Herpes Zoster (HZ) vaccine GSK1437173A in adults aged ≥70 years Primary publication: Cunningham AL, Lal H, Kovac M, Chlibek R, Hwang SJ, Díez-Domingo J, Godeaux O, Levin MJ, McElhaney JE, Puig-Barberà J, Vanden Abeele C. Efficacy of the herpes zoster subunit vaccine in adults 70 years of age or older.	End of study CSR (data lock point 12 October 2015) New England Journal of Medicine. 2016 Sep 15;375(11):1019-32.
ZOE-50/-70 (pooled analyses)	CSR: Included in ZOE-70 CSR – see above Primary publication: Pre-specified pooled efficacy data in ≥70 YOA included in primary publication for ZOE-70 – see above.	see above see above
	Supporting publication: Post-hoc immunogenicity data in ≥50 YOA pooled and by age strata: Cunningham AL, Heineman TC, Lal H, Godeaux O, Chlibek R, Hwang SJ, . . . Levin MJ. Immune responses to a recombinant glycoprotein e herpes zoster vaccine in adults aged 50 years or older.	Journal of Infectious Diseases. 2018; 217(11): 1750-1760.
ZOSTER-049 / ZOE-LTFU (NCT02723773)	A phase IIIb, open-label, multi-country, multi-centre, long-term follow-up study (ZOE-LTFU) of studies 110390 and 113077 (ZOSTER-006/022) to assess the prophylactic efficacy, safety, and immunogenicity persistence of GSK Biologicals' Herpes Zoster subunit (HZ/su) vaccine and assessment of 1 or 2 additional doses on a 0 or 0, 2-month schedule in two subgroups of older adults.	Final CSR (data lock point 01 December 2023)
	Primary publication: Strezova A, Domingo JD, Cunningham AL, Eto T, Andrews C, Arns C, Choo EJ, Hui DS, Icardi G, McNeil SA, Põder A. Final analysis of the ZOE-LTFU trial to 11 years post-vaccination: efficacy of the adjuvanted recombinant zoster vaccine against herpes zoster and related complications. [final analysis; data lock point 1 December 2023] Supporting publication: Boutry C, Hastie A, Diez-Domingo J, Tinoco JC, Yu CJ, Andrews C, Beytout J, Caso C, Cheng HS, Cheong HJ, Choo EJ. The adjuvanted recombinant zoster vaccine confers long-term protection against herpes zoster: interim results of an extension study of the pivotal phase 3 clinical trials ZOE-50 and ZOE-70. [first interim analysis; data lock point 30 July 2019] Supporting publication:	eClinicalMedicine. 2025 May 1;83. Clinical Infectious Diseases. 2022 Apr 15;74(8):1459-67.

Trial ID	Protocol title/ Publication title	Publication citation
	Strezova A, Diez-Domingo J, Al Shawafi K, Tinoco JC, Shi M, Pirrotta P, Mwakingwe-Omari A. Long-term protection against herpes zoster by the adjuvanted recombinant zoster vaccine: interim efficacy, immunogenicity, and safety results up to 10 years after initial vaccination. [second interim analysis; data lock point 19 August 2021]	In Open Forum Infectious Diseases 2022 Oct 1 (Vol. 9, No. 10, p. ofac485). US: Oxford University Press.

Source: Compiled from: Table 2-4: Trials (and associated reports) presented in the submission, pp71-72 of the submission; Table 2 5: A summary of the supporting documentation and location of results for studies included in this submission, p75 pf the submission.
Text in blue indicates trials or publications previously presented to PBAC.

6.11 The key features of the included evidence are summarised in Table 3.

Table 3: Key features of the included evidence: RZV versus placebo

Trial	N	Design/ duration	Risk of bias	Patient population	Outcome(s)	Use in modelled evaluation
RZV vs placebo (RCTs)						
ZOE-50	15,411	R, OB, MC, 3.2 years (mean, efficacy mTVC)	Low	Healthy individuals aged ≥ 50 years (mean 62.3 years)	Vaccine efficacy against HZ Vaccine efficacy against PHN, HZ complications, HZ mortality, HZ hospitalisations, HZ pain, immunogenicity and reactogenicity, EQ-5D	Vaccine efficacy from pooled ZOE-50/-70+ ZOSTER-049 estimate
ZOE-70	13,900	R, OB, MC, 3.7 years (mean, efficacy mTVC)	Low	Healthy individuals aged ≥70 years (mean 75.6 years)	As above	As above
RZV single arm extension study						
ZOSTER-049 [Final analysis]	7,529[a]	SA, OL, MC, 11.4 years post-vaccination (median, mTVC)	Serious[b]	As above; from ZOE-50/-70 RZV participants only	Vaccine efficacy against HZ Vaccine efficacy against PHN, non-PHN complications	Vaccine efficacy in terms of reduction in the incidence of HZ

Source: Compiled from Table 4: Key features of the included evidence, para 6.9 Public Summary Document (PSD) RZV March 2023 PBAC Meeting;
Synopsis, pp4-39 ZOSTER-049 CSR.
MC = multi-centre; mTVC: modified total vaccinated cohort (excluded those who did not receive a second vaccine dose or who had confirmed HZ within 1 month after the second dose); OB: observer blind; OL = open label; R = randomised; SA = single arm; TVC : total vaccinated cohort.
a The N=7,529 analysis set was defined as the TVC. Analyses were conducted using the N=7,273 modified TVC or N=7,258 subset thereof.
b Risk of bias based on ROBINS-I. Incorrectly noted to be 'low' when considered in March 2023.
Text in blue indicates trials previously presented to PBAC.

6.12 The ZOSTER-049 trial was a single arm study and employed historical controls derived from the observed values of the placebo arms in the ZOE-50/-70 parent studies for the analysis.

6.13 The ZOSTER-049 trial was at serious risk of bias due to multiple factors, including those identified by the ATAGI (missing data, absence of a placebo group, participant selection/exclusion from the study, and confounding due to difference in baseline risk between the vaccinated cohort and the historical control group) (ATAGI advice, April 2025) and further aspects raised in the evaluation (selection bias in the modified total vaccinated cohort [mTVC] analysis set; absence of an intent-to-treat analysis; attrition of subjects over time and inability to verify the historical controls construction or

methodology). The Pre Sub-Committee Response (PSCR) argued the ZOSTER-049 study is robust, reliable and in line with global standards, ensuring that differences in outcomes can be attributed to RZV.

Comparative effectiveness

6.14 The results of the ZOE-50/-70 trials for VE (HZ and PHN cases) were unchanged compared to the March 2023 submission.

6.15 Results of VE against HZ from the ZOSTER-049 study (primary outcome) at the final analysis (median 5.6 years post-vaccination at trial commencement to 11.4 years at completion) are presented in Table 4. The primary outcome of VE against HZ in the overall population was 79.77% (95% CI: 73.72, 84.61) in adults ≥50 years. VE in the 60-69 years cohort was 87.14% (95% CI: 74.17, 94.35).

Table 4: VE against HZ (Poisson regression): ZOSTER-049 (mTVC)

Trial	Age, y [1]	RZV [2]				Placebo / historical control [3]				VE_{HZ} % (95% CI)
		N	n	T (year)	IR_{HZ}/ 1,000 PYs	N	n	T (year) [4]	IR_{HZ}/ 1,000 PYs	
VE against HZ during ZOSTER-049 (median: 5.6 to 11.4 years post-vaccination)										
ZOSTER-049 (mTVC)	**Overall[5]**	7,258	69	39,109.3	1.8	7,258	341	39,109.3	8.7	79.77 (73.72, 84.61)
	50-59[6]	2,043	12	11,739.3	1.0	2,043	90	11,739.3	7.7	86.67 (75.55, 93.36)
	60-69[6]	1,242	9	6,957.4	1.3	1,242	70	6,957.4	10.1	87.14 (74.17, 94.35)
	≥70[6]	3,973	48	20,412.6	2.4	3,973	179	20,412.6	8.8	73.18 (62.94, 80.92)

Source: Table 2 23: Vaccine efficacy: First or only episode of HZ by age strata and overall using Poisson regression method (mTVC - pooled ZOE-50/-70 and mTVC – ZOSTER 049), p112 of the submission.

CI = confidence interval;; HZ = herpes zoster; IR = incidence rate; LTFU = long-term follow-up; mTVC = modified total vaccinated cohort; n = number of individuals having at least one confirmed herpes zoster episode; N = number of individuals included in each group; PY = person-year; RZV, recombinant zoster vaccine (*Shingrix*); T (year) = sum of follow-up (censored at the first occurrence of a confirmed HZ episode) expressed in years; VE = vaccine efficacy.

[1] Age strata defined by subjects' age at first vaccination in ZOE-50/-70 studies.

[2] Data from participants in the LTFU and control groups of the ZOE-LTFU study.

[3] Data from the placebo group of ZOE-50/70 were used to form the historical control. The number of participants (N) and follow-up period in the historical control were assumed to be the same as the vaccinated group. The n for historical controls represents the projected number of confirmed HZ episodes based on the estimated incidence rates using placebo group data of ZOE-50/70.

[4] Assumed to be the same as for RZV group from Year 6 onwards.

[5] Primary objective

[6] Secondary objective

6.16 VE against HZ by year since vaccination was reported for ZOSTER-049 as a secondary outcome are presented in Table 5 and Figure 1.

Table 5: VE against HZ by year since vaccination, ZOSTER-049 secondary outcome

Year	Age, years[1]	RZV [2]				Placebo / historical control [3]				VE_{HZ} % (95% CI)
		N	n	T (year)	IR_{HZ}/ 1,000 PYs	N	n	T (year) [4]	IR_{HZ}/ 1,000 PYs	
Y 1	Overall	13,881	3	13,744.5	0.2	14,035	130	13,823.3	9.4	97.68 (93.07, 99.53)
	50-59	3,491	1	3,462.9	0.3	3,523	31	3,475.0	8.9	96.76 (80.57, 99.92)
	60-69	2,140	0	2,125.3	0.0	2,166	16	2,142.1	7.5	100.00(79.32, 100.00)
	≥70	8,250	2	8,156.2	0.2	8,346	83	8,206.2	10.1	97.57 (90.96, 99.71)
Y 2	Overall	13,569	10	13,415.6	0.7	13,564	136	13,332.5	10.2	92.69 (86.15, 96.57)
	50-59	3,421	2	3,400.0	0.6	3,427	27	3,385.0	8.0	92.66 (70.78, 99.15)
	60-69	2,109	1	2,098.8	0.5	2,113	22	2,087.0	10.5	95.49 (72.11, 99.89)
	≥70	8,039	7	7,916.9	0.9	8,024	87	7,860.5	11.1	92.01 (82.82, 96.88)
Y 3	Overall	13,185	9	13,016.1	0.7	13,074	116	12,834.0	9.0	92.36 (84.98, 96.59)
	50-59	3,371	0	3,340.9	0.0	3,351	29	3,319.9	8.7	100.00(89.20, 100.00)
	60-69	2,078	0	2,063.1	0.0	2,062	29	2,025.7	14.3	100.00(89.39, 100.00)
	≥70	7,736	9	7,612.2	1.2	7,661	58	7,488.4	7.7	84.74 (68.99, 93.35)
Y 4	Overall	12,757	10	12,946.7	0.8	12,517	95	12,637.4	7.5	89.75 (80.31, 95.24)
	50-59	3,301	1	3,576.2	0.3	3,272	16	3,534.1	4.5	93.88 (60.62, 99.85)
	60-69	2,030	2	2,330.2	0.9	1,978	23	2,243.8	10.3	91.62 (66.10, 99.04)
	≥70	7,426	7	7,040.3	1.0	7,267	56	6,859.6	8.2	87.86 (73.30, 95.33)
Gap between ZOE-50/-70 and ZOSTER-049										
Y 6	Overall	7,258 (100%)	10	7,191.2	1.4	7258	62	7,191.2	8.6	83.87 (68.31, 92.63)
	50-59	2,043	2	2,032.8	1.0	2,043	16	2,032.8	7.9	87.5 (46.83, 98.61)
	60-69	1,242	1	1,233.1	0.8	1,242	13	1,233.1	10.5	92.31 (48.79, 99.82)
	≥70	3,973	7	3,925.3	1.8	3,973	35	3,925.3	8.9	80.00 (54.30, 92.50)
Y 7	Overall	7,083 (97.6%)	10	6,976.4	1.4	7,083	61	6,976.4	8.7	83.61 (67.76, 92.51)
	50-59	2,020	1	2,008.6	0.5	2,020	15	2,008.6	7.5	93.33 (56.67, 99.84)
	60-69	1,222	2	1,213.3	1.6	1,222	13	1,213.3	10.7	84.62 (32.04, 98.31)
	≥70	3,841	7	3,754.6	1.9	3,841	33	3,754.6	8.8	78.79 (51.24, 92.08)
Y 8	Overall	6,857 (94.5%)	10	6,743.1	1.5	6,857	58	6,743.1	8.6	82.76 (65.98, 92.14)
	50-59	1,998	2	1,985.6	1.0	1,998	15	1,985.6	7.6	86.67 (42.67, 98.52)
	60-69	1,198	2	1,189.2	1.7	1,198	13	1,189.2	10.9	84.62 (32.04, 98.31)
	≥70	3,661	6	3,568.3	1.7	3,661	31	3,568.3	8.7	80.65 (52.91, 93.40)
Y 9	Overall	6,627 (91.3%)	15	6,466.5	2.3	6,627	57	6,466.5	8.8	73.68 (52.89, 86.16)
	50-59	1,977	5	1,950.0	2.6	1,977	15	1,950.0	7.7	66.67 (3.52, 90.52)
	60-69	1,181	3	1,158.5	2.6	1,181	11	1,158.5	9.5	72.73 (-3.24, 95.11)
	≥70	3,469	7	3,358.0	2.1	3,469	29	3,358.0	8.6	75.86 (43.69, 91.07)
Y 10	Overall	6,239 (86.0%)	15	6,034.3	2.5	6,239	53	6,034.3	8.8	71.70 (49.03, 85.18)
	50-59	1,908	0	1,895.2	0.0	1,908	15	1,895.2	7.9	100 (77.89, 100)
	60-69	1,122	1	1,098.5	0.9	1,122	10	1,098.5	9.1	90.00 (29.71, 99.77)
	≥70	3,209	14	3,040.6	4.6	3,209	27	3,040.6	8.9	48.15 (-2.41, 74.87)
Y 11	Overall	5,849 (80.6%)	9	5,697.7	1.6	5,849	50	5,697.7	8.8	82.00 (63.03, 92.22)
	50-59	1,883	2	1,867.1	1.1	1,883	15	1,867.1	8.0	86.67 (42.67, 98.52)
	60-69	1,075	0	1,064.7	0.0	1,075	10	1,064.7	9.4	100.00(65.07, 100.00)
	≥70	2,891	7	2,765.9	2.5	2,891	25	2,765.9	9.0	72.00 (33.41, 89.77)

Source: Adapted from Table 2 24: Vaccine efficacy: First or only episode of HZ over each year of follow-up since one month post-dose 2 in ZOE-50/-70 studies by age strata and overall using Poisson regression method (mTVC - pooled ZOE-50/-70 and mTVC – ZOSTER-049), p115-116 of the submission.
CI = confidence interval; HZ = herpes zoster; IR = incidence rate; mTVC = modified total vaccinated cohort; n = number of individuals having at least one confirmed herpes zoster episode; N = number of individuals included in each group; PY = person-year; RZV, recombinant zoster vaccine (*Shingrix*®); T (year) = sum of follow-up (censored at the first occurrence of a confirmed HZ episode) expressed in years; VE = vaccine efficacy.
Text in blue indicates information previously presented to PBAC.

Figure 1: VE against HZ by year in ZOE-50/70 to the end of the ZOE-LTFU study (mTVC) (overall population)

Source: Figure 3, Strezova 2025
CI = confidence intervals; HZ = herpes zoster; mTVC = modified total vaccinated cohort (participants receiving 2 doses without confirmed HZ within 30 days post-dose 2); VE = vaccine efficacy; Y = year.

6.17 When analysed by age strata at vaccination and by year since vaccination (Table 5), the submission commented that VE_{HZ} appears to remain high over years 6-11, although confidence intervals were wide due to low HZ case numbers particularly in the younger age strata. The VE point estimates for individual age strata became variable with wider confidence intervals within each additional year of analysis, particularly from year 9 onwards. These fluctuations observed beyond Year 9 add uncertainty in the interpretation of evidence. Participant numbers reduced over time, with 86.0% remaining at year 10 and 80.6% by year 11. Given the mean age at vaccination was 67 years, this was considered consistent with a population approaching around 80 years. The ATAGI noted the reduction in VE after year 8 and then the apparent re-bound in year 11, and concluded that overall, there was a clear declining trend in VE, with variability in VE at the later time points (April 2025, p59). Additionally, ATAGI noted (April 2025, p43) that the decline between Years 9 and 10 coincided with an increase in HZ cases in the RZV arm (15 cases annually, up from 10 cases in prior years). This is not consistent with the claimed plateau in VE over time.

6.18 A key issue identified by ATAGI was "There is uncertainty regarding vaccine effectiveness beyond 11.4 years and when a booster dose may be required" (ATAGI

advice, April 2025). The ESC noted this remained an issue for interpretation of the clinical evidence in the evaluation particularly the durability of VE over time.

6.19 PHN and non-PHN complications during the ZOSTER-049 study were rare. Of the 69 HZ cases, five individuals developed complications (4 PHN and 1 disseminated HZ). These complications were observed in adults with an onset of HZ at >75 years and occurred 6-10 years after vaccination.

6.20 Results for VE against PHN for the overall population and by age strata for the trial period are presented in Table 6 VE_{PHN} in participants vaccinated at ≥50 years was 87.5% (95% CI: 64.8, 96.8) during the ZOSTER-049 trial period. VE_{PHN} in the 60-69 years cohort was 50.0% (95% CI: -860.45, 99.15) in the ZOSTER-049 trial period, noting the point estimate and confidence intervals were affected by there being only one PHN case reported. Overall, low cases of PHN meant that VE_{PHN} particularly for the 50-59 YOA and 60-69 YOA strata were variable with wide confidence intervals.

Table 6: VE against PHN (Poisson regression): ZOSTER-049 (mTVC)

Trial	Age strata[1]	RZV group[3]				Historical control[4]				VE_{PHN} % (95% CI)
		N	n	T(year)	n/T (per 1000)	N[2]	n	T(year)[2]	n/T (per 1000)	
VE against PHN during ZOSTER-049 (median: 5.6 to 11.4 years post-vaccination)										
ZOSTER-049 (mTVC)	**Overall**	7271	4	39347.3	0.1	7271	32	39347.3	0.8	87.50 (64.75, 96.79)
	50-59	2046	0	11795.6	0.0	2046	7	11795.6	0.6	100.00 (46.59, 100.00)
	60-69	1243	1	6986.1	0.1	1243	2	6986.1	0.3	50.00 (-860.45, 99.15)
	≥70	3982	3	20565.7	0.1	3982	23	20565.7	1.1	86.96 (56.83, 97.49)

Source: Table 2 26: Vaccine efficacy: First or only episode of PHN by age strata and overall using Poisson regression method (mTVC-pooled ZOE-50/-70 and mTVC-ZOSTER-049), p117 of the submission.

CI = confidence interval; DLP = data lock point; FU = follow-up; LTFU = long-term follow-up; mTVC = modified total vaccinated cohort; n = number of individuals having at least one confirmed herpes zoster episode; N = number of individuals included in each group; PHN = post herpetic neuralgia; PY = person-year; RZV = recombinant zoster vaccine (*Shingrix*); T (year) = sum of follow-up (censored at the first occurrence of a confirmed PHN episode) expressed in years; VE = vaccine efficacy.

[1] Age strata defined by subjects' age at first vaccination in ZOE-50/-70 studies.

[2] Assumed to be same as for RZV group in ZOSTER-049.

[3] Subjects from the RZV group in ZOE-50/-70 were used for Year 1 through Year 4 and subjects from LTFU group in ZOSTER-049 were used for Year 6 onwards.

[4] Subjects from the placebo group in ZOE-50/-70 were used for Year 1 through Year 4 and a historical control group based on the placebo group in ZOE-50/-70 were also used for Year 6 onwards.

6.21 Results for VE against non-PHN complications for the overall population and by age strata for the trial period are presented in Table 7 noting that there was only one non-PHN complication recorded during the ZOSTER-049 trial period. VE against non-PHN complications in participants vaccinated at ≥50 years was 91.7% (95% CI: 43.7, 99.8) during the ZOSTER-049 trial period. As for VE_{PHN}, the single non-PHN complication reported meant that VE against non-PHN complications were variable with wide confidence intervals.

Table 7: VE against non-PHN complications (Poisson regression): ZOSTER-049 (mTVC)

Trial	Age strata[1]	RZV[3]				Placebo/Historical control[4]				VE % (95% CI)
		N	n	T (year)	n/T (per 1000)	N[2]	n	T (year)[2]	n/T (per 1000)	
VE against HZ-related complications during ZOSTER-049 (median: 5.6 to 11.4 years post-vaccination)										
ZOSTER-049 (mTVC)	Overall	7273	1	39359.9	0.0	7273	12	39359.9	0.3	91.67 (43.68, 99.81)
	50-59	2046	0	11795.6	0.0	2046	0	11795.6	0.0	Undefined[5]
	60-69	1243	0	6986.3	0.0	1243	2	6986.3	0.3	100.00 (-247.21, 100.00)
	≥70	3984	1	20578.1	0.0	3984	9	20578.1	0.4	88.89 (19.81, 99.75)

Source: Table 2 27: Vaccine efficacy: First or only episode of HZ-related complications (other than PHN) by age strata and overall using Poisson regression method (mTVC-pooled ZOE-50/-70 and mTVC-ZOSTER-049), p119 of the submission

CI = confidence interval; DLP = data lock point; FU = follow-up; HZ = herpes zoster; LTFU = long-term follow-up; mTVC = modified total vaccinated cohort; n = number of individuals having at least one confirmed herpes zoster episode; N = number of individuals included in each group; PHN = post herpetic neuralgia; PY = person-year; RZV = recombinant zoster vaccine (*Shingrix*®); T (year) = sum of follow-up (censored at the first occurrence of a confirmed PHN episode) expressed in years; VE = vaccine efficacy

[1] Age strata defined by subjects' age at first vaccination in ZOE-50/-70 studies.

[2] Assumed to be same as for RZV group in ZOSTER-049.

[3] Subjects from the RZV group in ZOE-50/-70 were used for Year 1 through Year 4 and subjects from LTFU group in ZOSTER-049 were used for Year 6 onwards.

[4] Subjects from the placebo group in ZOE-50/-70 were used for Year 1 through Year 4 and a historical control group based on the placebo group in ZOE-50/-70 were also used for Year 6 onwards.

[5] VE is mathematically undefined when 0 cases observed in the historical control group

6.22 The ATAGI presubmission advice noted that, overall, the long-term immunogenicity data from ZOE-50/70 and ZOSTER-049 confirmed that RZV induces and maintains both humoral and cellular immunity at levels well above baseline for at least a decade post-vaccination. The advice noted that while younger participants (50–69 YOA) demonstrated slightly higher peak responses, the sustained plateau observed in older adults (≥70 YOA) still indicates meaningful immunogenicity, although there is no correlate of protection.

6.23 The March 2023 submission included four observational studies representing real world evidence of RZV use in practice (Izurieta et al, 2021; Lu et al, 2021, Sun et al, 2021b, 2021a). Three additional observational studies were included in the submission which provided new RWE for RZV vaccine effectiveness (VEff) in broad populations of adults largely without an increased risk of HZ (Florea et al, 2024; Tseng et al, 2025; Zerbo et al, 2024b, 2024a). The submission commented that although VEff against HZ reported in RWE studies was lower than those from the ZOE-50/-70 pooled analysis, that it was generally higher than in Izurieta et al, (2021) (70.1%; [95% CI: 68.6, 71.5]). Aside from Izurieta et al, (2021), the values of $VEff_{HZ}$ for the RWE ranged from 73.9% (95% CI: 71.8, 75.8) to 87.6% (95% CI: 78.9, 92.7) – thus the results for RWE were generally lower than observed in the trials. The PSCR noted the submission had provided justification for why lower estimates of $VEff_{HZ}$ from RWE are expected (primarily, differences in populations, including immunocompromised, as well as older, and possibly more frail subjects, as well as case ascertainment).

Comparative harms

6.24 The trial data regarding comparative harms remained essentially unchanged compared with the March 2023 submission. No new data or safety analyses were

presented for the ZOE-50/-70 trials. The ZOSTER-049 trial was a single arm design without comparative safety outcomes. The submission did not present additional adverse events (AE) data from the final analysis as it was not a key outcome for the study. Compared to the previous ZOSTER-049 interim analysis presented in the March 2023 submission, reporting of AEs up to completion of the trial was limited to serious adverse events (SAEs) which were judged to be unrelated to vaccination. The evaluation considered this was consistent with a population of advancing age with a relatively high baseline incidence of co-morbidities.

6.25 In terms of extended assessment of harms, a signal for events of Guillain-Barré syndrome (GBS) triggered an update to the TGA-approved Product Information (PI) to include GBS as a very rarely reported post marketing adverse reaction (update of August 2024) and to include relevant findings on which this was based from Goud et al, 2021 and the EPI-ZOSTER-032 trial (update of August 2025). Both studies reported a statistically significant increased risk of GBS in adults aged ≥65 years within a 42-day window following any dose of RZV, estimated at either 3 extra cases (Goud et al, 2021) or 7 extra cases (EPI-ZOSTER-032)[8] per million RZV doses administered. The ESC noted vertigo has also emerged as a rare adverse event.

Benefits/harms

6.26 A summary of the comparative benefits and harms for RZV versus vaccination at ≥50 years and 60 to 69 years is presented in Table 8.

[8] EPI-ZOSTER-032 (EMA real-world data entry): https://catalogues.ema.europa.eu/node/3357/resources

Table 8: Summary of comparative benefits/harms for RZV vs placebo (≥50 years i.e. all participants and 60-69 y)

Outcome/Trial	N	VE, % (95% CI)	Event rate/year/1,000 individuals vaccinated		Increment (per year/ 1,000 individuals)
			RZV	PBO	
Benefits					
Reduction in HZ cases (overall – ≥50 y)					
ZOSTER-049	14,516	79.77 (73.72, 84.61)	1.8	8.7	-6.9
Reduction in HZ cases (60-69 y)					
ZOSTER-049	2,484	87.14 (74.17, 94.35)	1.3	10.1	-8.8
Reduction in PHN cases (overall – ≥50 y)					
ZOSTER-049	14,452	87.50 (64.75, 96.79)	0.1	0.8	-0.7
Reduction in PHN cases (60-69 y)					
ZOSTER-049	2,486	50.00 (-860.45, 99.15)	0.1	0.3	-0.2
Reduction in non-PHN complications (overall – ≥50 y)					
ZOSTER-049	14,546	91.67 (43.68, 99.81)	0.0	0.3	-0.3
Reduction in non-PHN complications (60-69 y)					
ZOSTER-049	2,486	100.00 (-247.21, 100.00)	0.0	0.3	-0.3
Harms					
Event/trial	**RZV, n/N**	**PBO, n/N**	**RR (95% CI)**	**Event rate/1,000 individuals vaccinated**	**RD/1,000 individuals vaccinated**
				RZV / PBO	
Pain, Grade 3					
Pooled ZOE-50/-70	557/14,645	29/14,660	19.23 (NR)	38.03 / 1.98	36.06
Injection site erythema (any)					
Pooled ZOE-50/-70	1,357/14,645	37/14,660	36.71 (26.50, 52.37)	92.66 / 2.52	90.14
Injection site swelling (any)					
Pooled ZOE-50/-70	1,014/14,645	22/14,660	46.14 (30.30, 73.96)	69.24 / 1.50	67.74
Serious adverse events, at least one symptom					
Pooled ZOE-50/70	1,482/14,645	1,525/14,660	0.97 (0.91, 1.05)	101.19 / 104.02	-2.83

Source: Compiled from:
Table 9: Summary of comparative benefits and harms for RZV and no vaccine, PSD, RZV, March 2023 PBAC.
Submission tables (Table 2-23, p112; Table 2-25, p117; Table 2-26, p117; Table 2 27, p119).
CI = confidence interval; HZ = herpes zoster; n = number of participants reporting data; N = total participants in group; NR = not reported; PBO = placebo; PHN = post-herpetic neuralgia; RD = risk difference; RR = relative risk; RZV = recombinant zoster vaccine SAE = serious adverse event; VE = vaccine efficacy.
a Follow-up for ZOSTER-049 participants was a total median duration since vaccination of 11.4 years.
Text in blue indicates information previously presented to PBAC.

6.27 On the basis of evidence presented in the submission, for every 1,000 individuals aged ≥50 years vaccinated with RZV versus placebo over a median post-vaccination duration of 11.4 years:

- The number of cases of HZ would reduce by approximately 7 per year.
- The number of cases of PHN would reduce by approximately 1 case per year
- The number of cases of complications other than PHN would reduce by approximately 1 case per year.

6.28 The ESC noted a similar reduction in cases for individuals aged 60 to 69 years.

6.29 Based on evidence considered by the PBAC at the March 2023 meeting, for every 1,000 individuals vaccinated with RZV versus placebo over a median duration follow-up of 4.4 years:

- Approximately 36 additional individuals would experience Grade 3 pain.
- Approximately 90 additional individuals would experience any injection site erythema.
- Approximately 68 additional individuals would experience any injection site swelling.

Clinical claim

6.30 The submission claimed vaccination at 60 – 64 years of age was superior in terms of effectiveness compared to no vaccination at 60 – 64 years of age. This claim was likely adequately supported but the magnitude of the effect was likely over-estimated, and the long-term durability of VE remains uncertain. The key concerns include the serious risk of bias in the key ZOSTER-049 trial providing long-term VE follow up due to multiple factors including use of historical controls in place of a placebo arm. The ESC noted the clinical claim does not explicitly capture the downstream effect of bringing vaccination forward to a younger population i.e., more cases in the older, more vulnerable population.

6.31 The submission claimed vaccination at 60 – 64 years of age was 'slightly' inferior in terms of safety compared to no vaccination at 60 – 64 years of age.

6.32 The PBAC considered that the claim of superior comparative effectiveness was reasonable.

6.33 The PBAC considered that the claim of inferior comparative safety was reasonable.

Economic analysis

6.34 The submission presented a cost-utility analysis comparing vaccination with RZV starting at age 60 compared with vaccination starting at age 65. The model structure is unchanged from the March 2023 submission. Compared to the March 2023 PBAC consideration, the key changes to the economic model include values applied for HZ incidence, 2-dose VE waning, baseline utility and differential HZ QALY losses The key components of the economic model are presented in Table 9.

Table 9: Summary of model structure, key inputs and rationale

Component	Summary
Treatments	RZV for non-Indigenous adults at age 60 vs RZV for non-Indigenous adults at age 65.
Time horizon	Lifetime with a maximum age of 100 years.
Outcomes	Primary: QALYs, direct healthcare costs Secondary: LYs, HZ cases, PHN cases, non-PHN HZ-related complications, HZ-related deaths Societal (supplementary): HZ-related productivity losses, indirect productivity costs
Methods used to generate results	Static multi-cohort Markov model using cohort expected values
Health states	No HZ or complications HZ Recurrent HZ PHN Non-PHN HZ-related complications (ocular, neurological, disseminated, cutaneous) Death (absorbing) – HZ-related or all-cause
Cycle length	One-year
Transition probabilities	Age-specific annual incidence of HZ – pooled BEACH (2006-13) [risk adjustment 60-69 YOA] and Qian (2021) Age-specific risk of developing PHN given a case of HZ – BEACH (2006-13) Age-specific risk of non-PHN HZ-related complications – Yawn (2007) Age-specific HZ-related mortality – Le and Rothberg (2015) Age-specific all-cause mortality – ABS (2024) RZV VE_{HZ} and VE_{PHN}: ZOE-50/-70 trials and ZOSTER-049 LTFU study (Final Analysis)
Extrapolation method	2-dose VE waning: annual VE_{hz} from the ZOE-049 trial was used to establish the 11.4-year median follow up period. Linear extrapolation was then applied beyond the follow up period. 1-dose VE waning: 5.4% annually in years 1-4 and 5.1% annually from years 5 onwards. Based on consistency with the March 2023 submission, in which waning was equated with ZVL waning rate.
Health related quality of life	Baseline utilities: Redwood (2024) HZ related disease: Curran (2017a), Gater (2014), Serpell (2014) Differential QALY loss per breakthrough HZ case: Gianelos (2024). The ESC noted the previous economic model did not assume different QALY loss for vaccinated and unvaccinated cases. Vaccine related AEs: Schmader (2019)

Source: Table 3-3, p161 of the submission,
ABS = Australian Bureau of Statistics; AE = adverse event; HZ = herpes zoster; ICER = incremental cost-effectiveness ratio; LTFU = long-term follow-up PHN = post-herpetic neuralgia; QALY = quality-adjusted life year; RZV = recombinant zoster vaccine; VE vaccine efficacy; ZVL = zoster vaccine live.

6.35 The submission presented a base-case model applying a discount rate of 3.5% for costs and outcomes. The reduced discount rate was favourable to the intervention. When a discount rate of 5% was applied the ICER increased from $15,000 to < $25,000 per QALY gained to $15,000 to < $25,000 (+[redacted]%). A revised base-case using a discount rate of 5% for costs and outcomes (consistent with PBAC Guidelines) is presented herein.

The PSCR reiterated the importance of using a lower discount rate for health technologies that have upfront costs and benefits that accrue over a long period.

Model Inputs: Incidence

6.36 HZ incidence in the economic model was based on a pooled estimate from MacIntyre (2015) and Qian (2021). This was revised from previous submissions, in which HZ incidence was based on Macintyre (2015) alone. ATAGI previously noted that "the magnitude of difference in the critical Australian HZ incidence data of MacIntyre (2015), Qian (2021), and Lin (2022), suggested that BEACH [MacIntyre] data may overestimate HZ incidence" (ATAGI pre-PBAC advice, 2022) and further suggested that incidence rates from MacItnyre (2015), Qian (2021), and Lin (2022) be combined to create a single pooled estimate. However, ATAGI acknowledged limitations of the Lin (2022) (MedicineInsight) data raised by the submission and noted that "due to the sponsor's concerns about the MedicineInsight data pooling the BEACH and Qian 2021 would be acceptable" (ATAGI pre-PBAC advice, April 2025).

6.37 The evaluation noted the pooled estimate (MacIntyre (2015) and Qian (2021) results in a lower incidence than the previous submission. However, HZ incidence remains uncertain and the variation in incidence estimates is a source of uncertainty and the economic model was highly sensitive to this parameter.

6.38 The incidence of PHN per case of HZ was based on MacIntyre (2015). The approach for estimating PHN incidence is unchanged from previous submission. The rates from MacIntyre (2015) were higher than international estimates identified in the literature review. ATAGI considered that "MacIntyre (2015) is the most recent Australian data. It seems reasonable to use this data. PHN incidence could be derived as a % of the HZ incidence (rather than the absolute PHN incidence)" (ATAGI pre-PBAC advice, October 2022). However, due to methodological issues associated with BEACH data, the incidence of PHN is likely to be an overestimate. PHN incidence was estimated per case of HZ. As the submission has applied a pooled estimate for HZ incidence, the absolute number of PHN cases in the economic model is lower than in previous submissions. Despite this, PHN incidence estimates remain overestimated in the economic model, which is favourable to the intervention.

Model inputs: compliance

6.39 The economic model applied a two-dose compliance estimate of 82% for both cohorts derived from data from the 3 post-marketing studies. The ATAGI AIR data reported that crude 2-dose completion was 79.7%. The submission noted that this calculation will underestimate series completion rates as it does not account for individuals who have received RZV within the previous 1-5 months and thus have not had an opportunity to receive the 2nd dose of RZV. The AIR data likely remain the most appropriate source of compliance data. The PSCR provided a revised economic model that assumed 2 dose compliance in individuals aged 60 to 64 years was 80.3% (compared to 82.0% in individuals aged ≥ 65 years) (see paragraph 6.63).

Model inputs: VE and Waning

6.40 A comparison of model inputs for one dose and two dose VE and waning is provided in Table 10.

Table 10: Summary of model inputs for 1-dose and 2-dose RZV previous vs current submission

Age group	Initial VE, % (95% CI)	Annual VE waning, % (95% CI)
1 dose of RZV (no change from previous submission)		
50-69 YOA	90.1 (58.9 – 98.9)	Year 1-4: 5.4 (4.6 – 6.6) Year 5+: 5.1 (4.1 – 6.0)
≥70 YOA	69.5 (24.9 – 89.1)	
2 doses of RZV		
ZOSTER-049 Final Analysis (approx. 11 years of follow-up) – revised base-case		
50-69 YOA	97.8 (93.0 – 100.0)	1.2 (0.3 – 2.3)
≥70 YOA	99.4 (92.6 – 100.0)	3.1 (1.5 – 5.0)
ZOSTER-049 1st Interim Analysis (approx. 7 years of follow-up) – previous inputs		
50-69 YOA	98.9 (94.0 – 100.0)	1.5 (0.0 – 3.4)
≥70 YOA	95.4 (89.7 – 100.0)	2.3 (0.3 – 4.4)

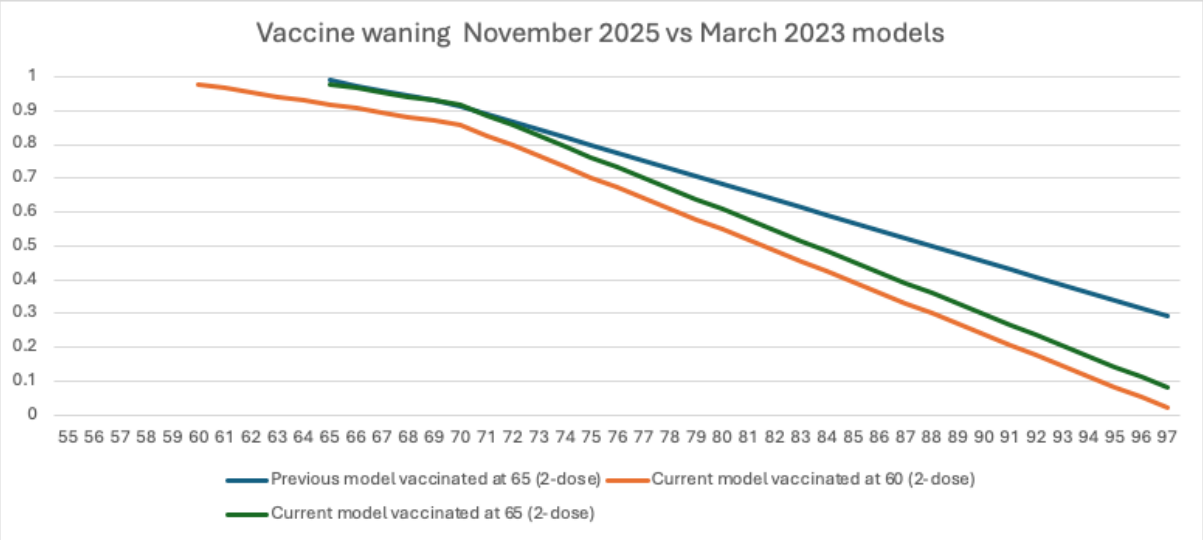
Source: Table 3-22, p212 of the submission.
CI, confidence interval; RZV, recombinant zoster vaccine; YOA, years of age.

6.41 Base-case model inputs for single-dose VE, including initial VE and VE waning were unchanged from previous submissions. The model was not sensitive to single dose assumptions given the assumed high 2-dose completion.

6.42 The submission incorporated updated data from ZOSTER-049 (median follow up 11.4 years) to determine initial 2 dose VE_{HZ} and waning. Initial 2 dose VE_{HZ} was assumed to be equal to the Y intercept of the regression line of best fit for VE_{HZ} waning. The initial two dose VE_{HZ} was 97.8% for adults aged 50-69 and 99.4% for adults aged 70 years or older.

6.43 The economic model assumed a linear waning function for 2-dose VE. The approach to waning was unchanged from the March 2023 PBAC submission, however the submission presented updated data from the Final Analysis of the ZOSTER-049 study (Figure 1), which has a longer follow-up than evidence presented in the previous submissions (median follow up approximately 11 years compared to approximately 8 years). The waning rates were revised based on these data. For adults 50-69 annual waning was decreased from 1.5% to 1.2%. For adults aged ≥70 the rate was increased from 2.3% to 3.1% (see Table 10). When the previous initial VE rates were combined with the previous VE_{HZ} waning (see Table 10) the ICER increased to $25,000 to < $35,000 (+[redacted]%).

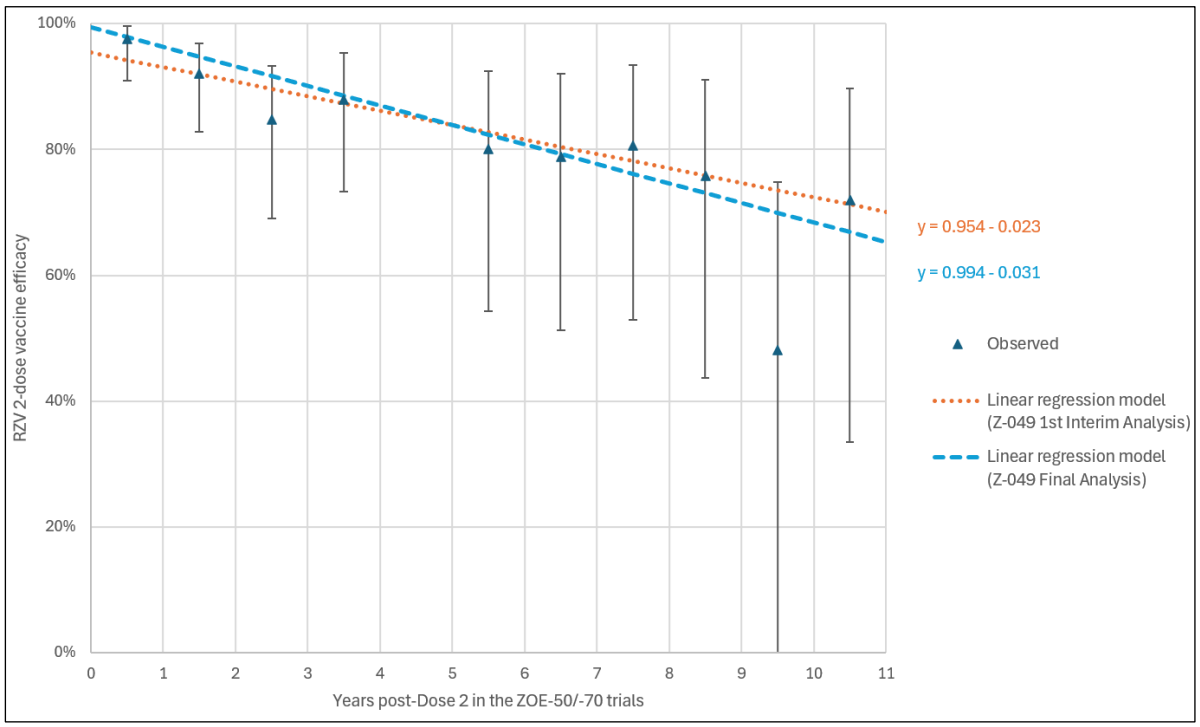
Figure 2: Vaccine waning in the November 2025 and March 2023 economic models



Source: Compiled during evaluation from Attachment 10a 'Shingrix 60-64 YOA – ZONA CEA

6.44 Figure 2 shows the waning function applied in the current economic model (green line vaccinated at 65 YOA, orange line at vaccinated 60 YOA) and the function applied in the March 2023 PBAC submission (blue line). The ESC noted the higher waning rate applied 5 years after vaccination for individuals vaccinated at 65 YOA and 10 years after vaccination for individuals vaccinated at 60 YOA. The submission claimed that the linear VE models remain a good fit to the observed data. Although the linear curve appears to approximate the data, Figure 3 highlights the width of the confidence intervals as the data follow up moves beyond 5-6 years but particularly beyond 8 years. The ESC noted Figure 3 was for individuals ≥ 70 YOA and the associated figure for individuals aged 60 to 69 years was not provided with the submission. The pre-PBAC response provided exemplary linear and non-linear regression functions fitted to annual VE for those vaccinated at 60 to 69 YOA and noted linear VE waning remained a reasonable but likely conservative assumption for individuals 60 to 69 YOA.

Figure 3: Comparison of observed yearly VE and linear models for adults ≥ 70 years of age at initial vaccination with RZV



Source: Figure 3-9, p220 of the submission.
VE = vaccine efficacy

6.45 The submission claimed that the approach used to generate the base case extrapolation was conservative based on two key assumptions: (i) VE waning plateauing, and (ii) lack of adjustment in the historical cohort arm of the ZOSTER -049 trial.

6.46 The submission claimed that the data demonstrated a plateauing of VE waning in years 10-11, which would mean that a linear function would overestimate VE waning. As discussed in paragraph 6.17, the ATAGI considered there was clear declining trend in VE, with variability in VE at the later time points. Furthermore, data pooling in years 11 and 12 adds further uncertainty to the assumption of linearity for the waning function and could imply that other non-linear waning functions may plausibly fit the data. The PSCR provided example regression functions fitted to ZOSTER-049 data and noted nearly all models predicted more optimistic long-term VE than using a simple linear model. The ESC noted VE from the ZOSTER-049 trial demonstrated a higher VE in year 11, which was inconsistent with the preceding trend, which showed a clear downward trajectory and considered this may impact on determining the best fit function. The ESC further noted the analysis in the PSCR was presented for individuals ≥ 50 YOA rather than individuals 60 to 69 YOA. The ESC noted the figures presented in the ATAGI pre-submission advice and considered it was unclear if a linear model would

be the best fit and what impact incorporating a different (non-linear) regression function may have on modelled results.

6.47 The economic model assumed that RZV does not offer additional protection against PHN in breakthrough cases, which implies breakthrough HZ cases in vaccinated person have the same probability of developing PHN as unvaccinated persons. The evaluation considered this assumption is reasonable and likely conservative. The PSCR provided a pooled analysis of currently available RWE that indicated RZV may provide direct protection against PHN, further supporting the conservative nature of the assumption.

6.48 The historical cohort in ZOSTER-049 did not account for ageing or presence of comorbidities. The submission assumed therefore, that the number of HZ cases in the control arm may have been underestimated, which would lead to underestimated VE in the intervention arm of the ZOSTER-049 trial. This assumption does not appear reasonable. ATAGI noted that it did "not consider the base-case VE projection proposed by the sponsor to be conservative… The sensitivity analysis for overall VE with age adjustment in historical control construction had similar results compared with primary VE analyses'" (ATAGI pre-PBAC advice, April 2025). As an alternative to using historical controls in the ZOSTER-049 study, the PSCR presented a naïve comparison of the ZOSTER-049 vaccinated cohort versus an age-matched HZ incidence gradient from a natural history study undertaken by Curran (2022). The PSCR stated this analysis demonstrated that, in the absence of adjustment for prognostic factors associated with age and accumulating comorbidities, the incidence rate (IR) of HZ in the HC arm decreased over time, while the IR_{HZ} in the natural history arm increased with age as expected. The PSCR stated this demonstrates that the HC arm likely underestimated HZ incidence and the lack of adjustment for ageing in the HC arm likely led to significant underestimation of long-term VE and overestimation of associated VE waning. The ESC noted that the incidence of HZ over time was not the only characteristic of the historical control group considered likely to contribute to uncertainty in the overall VE and considered the uncertainty regarding VE_{HZ} remained.

6.49 Despite the availability of long-term follow up data from the ZOSTER -049 trial, vaccinated individuals in the model maintain coverage for long periods of time i.e. approximately 50% at 20 years. The ESC noted that, as the proposed population are younger than the current population, they are more likely to survive longer periods with lower vaccine coverage. The ESC noted ATAGI considered predicting waning effects over 40 years based on 11 years of ZOSTER-049 data introduces significant uncertainty (ATAGI pre-submission advice, April 2025).

6.50 The economic model assumed a higher rate of waning starting at age 70 based on the observation that VE_{HZ} waned at a faster rate in those vaccinated at ≥70 YOA when compared to those vaccinated at 50-69 YOA. However, the submission further noted that there was no evidence from ZOSTER-049 that an individual vaccinated at a younger age would experience faster waning when they reach the age of 70 YOA. When the waning rate from the 60–69-year-old cohort was applied for the whole

population the ICER decreased from $15,000 to < $25,000 per QALY gained to $15,000 to < $25,000 (-[redacted]%). When a midpoint estimate (2.15%) was applied the ICER increased to $35,000 to < $45,000 (+[redacted]%).

6.51 The base case VE waning estimates applied in the model are highly uncertain and are a key driver of the economic model. The ESC considered it was uncertain if applying different waning rates to individuals < 70 YOA and ≥ 70 YOA was reasonable, noting this resulted in a shorter period of time before the higher waning rate was applied for individuals vaccinated at 65 YOA compared to those vaccinated at 60 YOA. Additionally, the ESC considered it remained uncertain if a linear waning model was reasonable for individuals vaccinated 60 to 69 YOA. The ESC noted that the proposed population are younger than previously listed, and are more likely to survive longer periods with lower vaccine coverage.

Health Outcomes

6.52 Baseline utilities in the economic model were revised based on a recent study by Redwood (2024) and valued using Norman (2023).

6.53 QALY losses per (unvaccinated) case of HZ and PHN were unchanged from previous submissions. The ESC previously considered the QALY loss per case of HZ and PHN were overestimated (paragraph 6.56 RZV PSD, March 2023 PBAC meeting). The ESC noted the model was sensitive to QALY loss per HZ and PHN case. The ESC noted that higher utility decrements for older people experiencing HZ and PHN were included in the model; however, it is unclear if the difference adequately captures the more serious sequelae that can be experienced by older cohorts. The ESC considered shifting the vaccination age lower could result in more serious cases of HZ and PHN in the older cohorts and not adjusting for this appropriately in the model could overestimate QALY gains and underestimate the ICER.

Table 11: Estimated QALY loss per HZ and PHN case applied in the model for unvaccinated individuals

	Utility loss	Duration (months) [a]	QALY loss
Per HZ case			
50-59 YOA	0.173	1.61	0.02328
60-69 YOA		1.60	0.02306
70-79 YOA		1.68	0.02421
≥80 YOA		1.71	0.02462
Per PHN case			
50-69 YOA	0.211	10.3	0.1811
≥70 YOA		12.9	0.2268

Source: Table 3-30, p237 of the submission

HZ = herpes zoster; PHN = post-herpetic neuralgia; QALY = quality-adjusted life year.

[a]HZ duration calculated per Curran (2017) methodology, applying the Australian-based % of HZ cases which develop PHN. PHN duration is sourced from the SPS trial, as reported in a cost-effectiveness analysis of live zoster vaccine

6.54 The submission applied differential HZ QALY losses according to whether an individual had received RZV vaccination or not. This was an updated assumption for this submission and was not applied in the previous submission. Vaccinated individuals incurred a QALY loss that was approximately 65% lower than unvaccinated individuals. The submission supported their claim with a recent meta-analysis from Giannelos

(2024). While the studies included in Giannelos (2024) appear to favour vaccinated individuals, the key driver of the favourable effect in the direction of vaccinated individuals appears to be the ZOE-HSCT study, which looked specifically at individuals recovering from hematopoietic stem cell transplant, which is not representative of the proposed population. The PSCR noted a re-analysis excluding the ZOE-HSCT study predicted a 55% lower QALY loss in vaccinated individuals (compared to 65% in the base case). The PSCR presented a revised economic model based on this assumption (see paragraph 6.636.62). The ESC noted a sensitivity analysis assuming no difference in QALY losses for vaccinated and unvaccinated individuals increased the ICER by [redacted]%.

Resource Use

6.55 Vaccine administration costs applied in the model were lower than those presented in the March 2023 consideration. The submission stated that administration of the first dose is relatively easy to combine with another medical intervention when administered in a GP setting, whereas the second dose administration is more likely to merit a stand-alone intervention specifically for this purpose. Therefore, in the GP setting, it was assumed that vaccine administration cost would be reduced by 50% for the first dose of RZV, but a stand-alone consultation would be required for administration of the second dose of RZV and would incur the complete cost. It may be likely that some individuals will attend GP clinics with the specific intention of receiving RZV. Furthermore, GP attendance is likely to be higher in the older cohort, so changing the assumption when the proposed listing population is younger, may underestimate vaccine administration costs. In the March 2023 submission, a more conservative assumption was applied which assumed the cost of administration for both doses was equal. When the first and second GP administration prices were adjusted in the model to be consistent with the previous submission ($18.20 per dose)) the ICER increased from $15,000 to < $25,000 per QALY gained to $25,000 to < $35,000 (+[redacted]%). The ESC considered the assumptions regarding administration costs were poorly supported.

6.56 The costs associated with disease management per case of HZ, PHN, or other complications were estimated by applying unit cost estimates from relevant publicly available sources (PBS, National Hospital Cost Data Collection [NHCDC] Public Sector Report 2022-23) to incidence-adjusted (MacIntyre, 2015) rates for GP visits, ED visits, and hospitalisations per HZ and HZ with PHN cases from a US-based study (Yawn, 2009. Given the assumptions involved in this adjustment, there is some uncertainty. Firstly, as discussed, MacIntyre (2015) data may overestimate the rate of PHN per case of HZ. Secondly, Yawn et al. (2009) was based in Minnesota in the US and data are now 24 years old. It is plausible that resource utilisation and clinician behaviour may have changed over this period and may be different in the Australian healthcare system. The ESC previously noted that “a reduction in costs associated with HZ cases, PHN cases and non-PHN complications accounted for a high proportion of the cost offsets in the economic model” (para 6.58, RZV, PSD, March 2023 PBAC meeting). Despite this, the per-case cost of HZ did not appear to be a key driver of the economic model.

For illustrative purposes, sensitivity analysis conducted during the evaluation tested costs per HZ case adjusted by +/-20% led to changes in the ICER from $15,000 to < $25,000 per QALY gained to $15,000 to < $25,000 (-[redacted]%) and $25,000 to < $35,000 (+[redacted]%) respectively. When the costs per case of PHN were adjusted +/- 20% the ICER changed to $15,000 to < $25,000 (-[redacted]%) and $25,000 to < $35,000 (+[redacted]%) respectively.

6.57 Key drivers of the economic model are provided in Table 12.

Table 12: Key drivers of the model

Description	Method/Value	Impact Base case: $[redacted][1]/QALY gained
Waning of VE	Linear regression based on annual VE_{HZ} in the ZOSTER-049 trial. Different waning rates were applied to individuals 60 to 69 YOA and ≥ 70 YOA	Very high, favours intervention. Applying a higher rate of waning (2.15%) to whole cohort, increased ICER to $[redacted][2] (+[redacted]%)
Incidence of HZ	Pooled midpoint estimate from MacIntyre (2015) and Qian (2021).	High When lower rates from Qian (2021) were applied in the economic model the ICER increased to $[redacted][3]/QALY (+[redacted]%).
QALY loss per HZ case	Estimated utility loss per case of HZ (Gater (2014) and Serpell (2014)) was multiplied by mean duration of HZ case without PHN from Curran (2017) assuming an exponential decay in disutility.	High In sensitivity analysis conducted during the evaluation, when the lowest literature estimate was applied (Pieters (2022)) the ICER increased to $[redacted][3] (+[redacted]%). When the highest literature estimate, (de Boer (2019)) was applied the ICER decreased to $[redacted][4] (-[redacted]%)
QALY loss per PHN case	Estimated utility loss per case of HZ (Gater (2014) and Serpell (2014)) was multiplied by mean duration of HZ case in the SPS trial (Moore 2010).	High In sensitivity analysis conducted during the evaluation, when the lowest literature estimate was applied the ICER increased to $[redacted][3] (+[redacted]%). When the highest literature estimate, was applied the ICER decreased to $[redacted][1] (-[redacted]%).
Discount rate	5% (base case presented in the evaluation, base case applied in the submission was 3.5%)	High, lower rate applied favoured intervention When a rate of 3.5% was applied the ICER decreased to $[redacted][1] (-[redacted]%) and when no discounting was applied the intervention became dominant.

Source: Compiled during evaluation

HZ = herpes zoster; ICER = incremental cost-effectiveness ratio; PHN = post-herpetic neuralgia; QALY = quality-adjusted life year; VE = vaccine efficacy

The redacted values correspond to the following ranges:

[1] *$15,000 to < $25,000*

[2] *$35,000 to < $45,000*

[3] *$25,000 to < $35,000*

[4] *$5,000 to < $15,000*

6.58 The results of the economic evaluation for RZV vaccination starting at age 60 compared to RZV starting at age 65 are presented in Table 13.

Table 13: Results of economic evaluation for RZV vaccination at age 60 compared to RZV at age 65

Result	RZV 60 YOA	RZV 65 YOA	Δ abs.	Δ rel.	% of incr. diff.
Case counts per million vaccinated (undiscounted)					
HZ cases	147,505	181,911	-34,406	-19%	-
PHN cases	34,429	38,470	-4,042	-11%	-
Non-PHN complications cases	23,214	25,962	-2,748	-11%	-
Ocular	8,620	9,944	-1,324	-13%	-
Neurological	7,435	8,263	-827	-10%	-
Cutaneous	3,552	3,770	-218	-6%	-
Other non-pain	3,607	3,986	-378	-9%	-
HZ-related deaths	23,322	22,931	+0	+2%	-
Costs (discounted)					
Total direct costs	$[redacted]	$[redacted]	+$[redacted]	+[redacted]%	+[redacted]%
Vaccine-related	$[redacted]	$[redacted]	+$[redacted]	+[redacted]%	+[redacted]%
Vaccine acquisition	$[redacted]	$[redacted]	+$[redacted]	+[redacted]%	+[redacted]%
Vaccine administration	$[redacted]	$[redacted]	+$[redacted]	+[redacted]%	+[redacted]%
Vaccine-related AEs	$[redacted]	$[redacted]	+$[redacted]	+[redacted]%	+[redacted]%
Disease-related	$[redacted]	$[redacted]	-$[redacted]	-[redacted]%	-[redacted]%
HZ cases	$[redacted]	$[redacted]	-$[redacted]	-[redacted]%	-[redacted]%
PHN cases	$[redacted]	$[redacted]	-$[redacted]	-[redacted]%	-[redacted]%
Non-PHN complications cases (All)	$[redacted]	$[redacted]	-$[redacted]	-[redacted]%	-[redacted]%
Outcomes (discounted)					
LYs	14,236,727	14,236,718	+9	+0%	+100%
QALYs	12,435,035	12,433,337	+1,698	+0%	+100%
Healthy QALYs lived	12,438,704	12,438,697	+8	+0%	+0%
Overall QALYs lost	-3,669	-5,359	+1,690	-32%	+100%
HZ	-795	-1,620	+825	-51%	+49%
PHN	-2,873	-3,739	+865	-23%	+51%
Vaccine-related AEs	-0.493	-0.355	-0.138	+39%	-0%
Incremental cost per QALY gained			$[redacted][1]		

Source: Economic model – attachment 10 "Shingrix 60-64 YOA – ZONA CEA"
AE = adverse event; HZ = herpes zoster; ICER = incremental cost-effectiveness ratio / cost per QALY; LY = life year; PHN = post-herpetic neuralgia; QALY = quality-adjusted life year; RZV = recombinant zoster vaccine.
The redacted value corresponds to the following range:
[1] $15,000 to < $25,000

6.59 These results should be interpreted with caution for the following reasons:

- Vaccine efficacy waning was generated using linear regression of annual VE presented in ZOSTER-049. These estimates were built on a diminishing sample with wide confidence intervals and therefore assumptions about the linearity of the waning function and the rate are uncertain. Additionally, the ESC noted the model assumed reduced protection for individuals vaccinated at 65 YOA than at 60 YOA with increased waning at 70 YOA in both models (see paragraph 6.44).
- Initial VE was estimated as the y-intercept of the same linear regression used to estimate vaccine waning and therefore is subject to the same uncertainty.

- HZ incidence while lower than presented in previous submissions may still represent a high estimate thus favouring the intervention.
- Utility loss per case of HZ and PHN. These were unchanged from previous submissions and likely represent an overestimate of QALY losses per case, which is favourable to the intervention.

6.60 The main cost which contributes to the ICER was from vaccine acquisition and administration. Cost savings from reduced disease related costs were observed, particularly for HZ cases avoided.

6.61 The base case estimated that there would be 34,406 fewer HZ cases and, 4,042 fewer PHN cases across the full time horizon of the model, the net impact of these avoided cases was an additional 1,690 QALYs per 1 million vaccinated adults. Vaccine related adverse events were not explicitly modelled, but the additional cost of treating vaccine related AEs was estimated at $1,814,715. Table 14 shows the disaggregated base case results per age group. These outcomes highlight that the improvements in health that drive the outcomes of the model almost all occur in the 60-64 YOA group. For every other age group the number of events that occurred in total is lower in those who received the vaccination at a later age. This was likely due to vaccine waning effects, whereby, those vaccinated at 60-64 would have lower VE by older ages, than those who received vaccination at age 65.

Table 14: Disaggregated base-case results for number of events per age group

Age group (years)	Number of events		Δ abs. (Δ rel.)	% of incr. diff.
	RZV at 60 YOA	RZV at 65 YOA		
HZ cases				
60-64	4,575	53,034	-48,459 (-91%)	141%
65-69	11,045	8,069	+2,975 (+37%)	-9%
70-79	48,509	41,458	+7,052 (+17%)	-20%
80-89	62,786	59,570	+3,215 (+5%)	-9%
≥90	20,591	19,780	+811 (+4%)	-2%
Total	**147,505**	**181,911**	**-34,406 (-19%)**	**100%**
PHN cases				
60-64	668	7,743	-7,075 (-91%)	175%
65-69	1,613	1,178	+434 (+37%)	-11%
70-79	10,779	9,212	+1,567 (+17%)	-39%
80-89	16,092	15,268	+824 (+5%)	-20%
≥90	5,277	5,070	+208 (+4%)	-5%
Total	**34,429**	**38,470**	**-4,042 (-11%)**	**100%**
Non-PHN complications				
60-64	451	5,228	-4,777 (-91%)	174%
65-69	1,089	795	+293 (+37%)	-11%
70-79	7,099	6,067	+1,032 (+17%)	-38%
80-89	10,976	10,413	+562 (+5%)	-20%
≥90	3,599	3,458	+142 (+4%)	-5%
Total	**23,214**	**25,962**	**-2,748 (-11%)**	**100%**

Source: Table 3-77, p302 of the submission, edited to reflect 5% discount rate using Attachment 10a. 60-64 YOA – ZONA CEA
abs. = absolute; AE = adverse event; HZ = herpes zoster; incr. = incremental; PHN = post-herpetic neuralgia; rel. = relative; RZV = recombinant zoster vaccine; Δ = delta / difference.

6.62 Disaggregated results from the economic model demonstrate that all the health benefits of bringing forward RZV vaccination to age 60 are accrued in those aged 60-64 (i.e. 48,459 fewer HZ cases per million people vaccinated). However, for all age groups 65 and above, earlier vaccination led to worse health outcomes (i.e. 14,053 additional HZ cases in those aged 65-100). The ESC also noted there would be an additional 4,027 HZ cases in individuals aged ≥ 80 years if individuals were vaccinated at 60 YOA. The pre-PBAC response noted the submission has weighed up the trade-offs of bringing forward vaccination to 60 YOA with substantial overall public health benefits apparent, with certainty of upfront prevention of HZ burden versus a future potential of increased cases at older ages.

6.63 The PSCR provided a revised economic model that (i) reduced 2 dose compliance in individuals aged 60 to 64 years to 80.3% (from 82.0% in the base case) and (ii) changed the proportion of QALY losses in vaccinated vs unvaccinated HZ cases to 44.7% (from 35.5% in the base case). This increased the ICER from $15,000 to < $25,000 (using a discount rate of 5%) to $25,000 to < $35,000 per QALY. The ICER using a discount rate of 3.5% was $15,000 to < $25,000 per QALY (compared to $15,000 to < $25,000 per QALY in the model provided in the submission). The ESC noted this model has not been evaluated.

6.64 The results of key sensitivity analyses compiled during the evaluation are presented in Table 15 below.

Table 15: Results of sensitivity analyses

Analyses	Incremental cost	Incremental QALY	ICER	% change from base-case
Base case	$[redacted]	1,698	$[redacted]1	-
Discount rate (base case 5% costs and outcomes)				
• 0% costs and outcomes	-$[redacted]	1,413	Dominant	-
• 3.5% costs and outcomes	$[redacted]	1,655	$[redacted]1	-[redacted]%
Incidence rates HZ (base case pooled MacIntyre (2015) and Qian (2021))				
• Rates from Qian (2021)	$[redacted]	1,390	$[redacted]2	+[redacted]%
• Rates from MacIntyre (2015)(1.259% for 60-64, 1.489% for 65-69, 1.531% for 70-79, 1.989% for ≥80)	$[redacted]	1,978	$[redacted]1	-[redacted]%
Initial 2-dose VE (base case 97.8% for 50-69, 99.4% for 70+)				
• Lower bound 95% CI	$[redacted]	1,605	$[redacted]2	+[redacted]%
• Upper bound 95% CI	$[redacted]	1,741	$[redacted]1	-[redacted]%
VE waning – 2-dose (base case 1.2% for 50-69, 3.1% for 70+)				
• Lower bound 95% CI	$[redacted]	2,087	$[redacted]3	-[redacted]%
• Upper bound 95% CI	$[redacted]	1,310	$[redacted]4	+[redacted]%
• Values in previous submission (1.5% for 50-69, 2.3% for 70+)	$[redacted]	1,598	$[redacted]2	+[redacted]%
• Waning rate for 50-69 for whole cohort	$[redacted]	1,742	$[redacted]1	-[redacted]%
• Waning rate for 70+ for whole cohort	$[redacted]	961	$[redacted]5	+[redacted]%
• Midpoint (2.15%) of cohort rate applied to whole cohort	$[redacted]	1,346	$[redacted]4	+[redacted]%
QALY loss per case HZ - unvaccinated (base case 0.23-0.26)				
• Lowest literature estimate (Pieters (2022)	$[redacted]	1,226	$[redacted]2	+[redacted]%
• Highest literature estimate (de Boer (2019))	$[redacted]	3,443	$[redacted]3	-[redacted]%
• -20%	$[redacted]	1,533	$[redacted]2	+[redacted]%
• +20%	$[redacted]	1,863	$[redacted]1	-[redacted]%
Differential QALY loss per case of HZ vaccinated vs unvaccinated (base vaccinated = 35.5% of unvaccinated)				
• Lower bound (11%)	$[redacted]	1,730	$[redacted]1	-[redacted]%
• Upper bound (100%)	$[redacted]	1,613	$[redacted]2	+[redacted]%
QALY loss per case of PHN (base case (0.18-0.22)				
• Lowest literature estimate (0.106)	$[redacted]	1,283	$[redacted]2	+[redacted]%
• Highest literature estimate (0.314)	$[redacted]	2,334	$[redacted]1	-[redacted]%
• -20%	$[redacted]	1,440	$[redacted]2	+[redacted]%
• +20%	$[redacted]	1,786	$[redacted]1	-[redacted]%
Multivariate analyses				
Upper bound of 2-dose waning function + no baseline difference in QALY loss per-HZ case between vaccinated and unvaccinated individuals	$[redacted]	1,219	$[redacted]4	+[redacted]%

Analyses	Incremental cost	Incremental QALY	ICER	% change from base-case
Upper bound of 2-dose waning function + no baseline difference in QALY loss per-HZ case between vaccinated and unvaccinated individuals + lower bound (-20%) of HZ and PHN QALY loss.	$[redacted]	981	$[redacted][6]	+[redacted]%

Source: compiled during the evaluation using the economic model attachment 10a"Shingrix 60-64 – ZONA CEA".
CI = confidence interval; GP = general practitioner; HZ = herpes zoster; ICER = incremental cost-effectiveness ratio; PHN = post-herpetic neuralgia; QALY = quality-adjusted life year; VE = vaccine efficacy.
The redacted values correspond to the following ranges:
[1] *$15,000 to < $25,000*
[2] *$25,000 to < $35,000*
[3] *$5,000 to < $15,000*
[4] *$35,000 to < $45,000*
[5] *$55,000 to < $65,000*
[6] *$45,000 to < $55,000*

6.65 The submission also presented an economic evaluation with a societal perspective incorporating indirect costs related to disease- and vaccine-related productivity losses using the same model as described above. The overall indirect costs due to productively losses (considering absenteeism only) were estimated to be $10.9 million for the 60-64 YOA arm and $26.3 million for the ≥65 YOA arm. The ICER considering a societal perspective was $15,000 to < $25,000 per QALY gained. The inputs to estimating productivity costs were based on a number of assumptions thus remain uncertain particularly in deriving data for those aged ≥65 YOA due to lack of granular data. Issues identified relating to uncertainty in the assumptions applied in the economic model (paragraph 6.59) similarly applies to the supplementary economic evaluation. The PSCR noted that adults aged 60 to 64 years of age mostly remain in the workforce (64%) compared to adults ≥65 years of age (16%) (ABS, 2024[9]). The PSCR stated HZ-related productivity impacts and potential broader economic benefits from a societal perspective are highly relevant for decision-making.

Vaccine cost/ person/course

6.66 The average cost of a course of RZV vaccination is $[redacted], assuming compliance of a 2 dose course is 82%[10].

Estimated PBS usage & financial implications

6.67 This submission was not considered by DUSC.

[9] *ABS. (2024). Labour Force, Australia, Detailed. December 2024. https://www.abs.gov.au/statistics/labour/employment-and-unemployment/labour-force-australia-detailed/latest-release*
[10] $[redacted] + 82% x $[redacted]

6.68 The submission used an epidemiological approach to estimate the utilisation and financial estimates of the proposed listing of 2-dose RZV for non-Indigenous adults aged 60-64.

6.69 The key inputs and sources for the financial estimates are presented in Table 16.

Table 16: Key inputs for financial estimates

Parameter	Value applied and source	Comment
Eligible population (aged 60-64)	Based on overall Australian population less: • (IC moderate risk (10.36% annual growth applied to September 2023 ATAGI advice; • IC high risk (2.35%-2.67% growth rate applied to September 2023 ATAGI advice); • First Nations Peoples aged 60-64 (ABS); • non-Indigenous who had received 2-doses (sponsor's private market data).	The overall approach applied in the submission appears reasonable, however, it was noted that: • The submission claimed that private market data were preferred as this was specific to the proposed NIP population (excludes individuals who are already NIP eligible either due to being an Aboriginal and/or Torres Strait Islander and/or being at moderate to severe increased risk of HZ). This appears reasonable. The PSCR provided revised financials that include a small increase to the proportion of individuals who have previously received 1 or 2 doses of RZV on the private market (see paragraph 6.71).
Uptake rate 1st dose in the already eligible population.	Yrs 1 - 2 were extrapolated using OLS regression from AIR data for uptake rates for non-Indigenous adults since NIP listing November 2023 – May 2025. Yrs 3-6 50% relative growth rate assumption based on the relative change in growth in 2025 compared to 2024 was 21.5% / 40.4% = 53.3%, which was assumed to remain a constant 50% from Year 3 to Year 6 of NIP eligibility based on UK data on HZ vaccine coverage in the UK by the end of June 2023 (UK Health Security Agency, 2024b)	This is uncertain and likely overestimated due to the data being from an older cohort who would likely receive more GP services and differences in healthcare systems.). The PSCR provided updated estimates of uptake in individuals ≥ 65 YOA (see paragraph 6.71).
Uptake rate for 1st dose for non-Indigenous adults aged 60-64	Assumption: 15% relative reduction in uptake compared to non-Indigenous adults ≥65	This assumption was inconsistent with ATAGI pre-submission advice which reported that a 20% relative reduction in uptake for those aged 60-64 compared to those ≥65, with sensitivity analyses of 15% and 25%, appeared reasonable (q10, p82, ATAGI pre-PBAC advice, April 2025). Yr 1: 34.3%, Yr 2: 52.6%, Yr 3: 61.8%, Yr 4: 66.4%, Yr 5:67.7%, Yr 6: 69.8% in submission The PSCR provided updated financials (see paragraph 6.71) assuming: Yr 1: 23.6%, Yr 2: 35.5%, Yr 3: 42.1%, Yr 4: 45.8%, Yr 5:47.7%, Yr 6: 48.8%
Second dose compliance	Assumption 82%	This rate was based completion rates reported across post-marketing studies in Canada and the USA (Ackerson et al., 2021; Cubanski et al., 2020; Dooling,

Parameter	Value applied and source	Comment
		2019; Izurieta et al., 2021; LaMori et al., 2022; McGirr et al., 2021; Patterson et al., 2022). It was updated from 80% applied previously in the March 2023 financial model. The PSCR provided revised financials assuming uptake of 80.3% in individuals aged 60 to 64 years (see paragraph 6.71)
HZ, PHN and non-PHN complication cases avoided	Results from the economic evaluation based on the number of events avoided per 1 million peoples who receive the first dose were used to determine cost saving to PBS (reduction in HZ related antivirals and PHN medications) and MBS (reduction in GP visits, ED visits and hospitalisations).	Based on these uncertainties in the economic model it is likely that the public health impacts of listing RZV for non-Indigenous adults aged 60-64 have been overestimated in the financial estimates, which is favourable to the intervention. A similar concern was noted in the March 2023 submission where it was noted that "these estimates may be overestimated as they were based on estimated reductions in the incidence of HZ, PHN and non-PHN complication from the economic model" (paragraph 6.78, RZV, PSD, March 2023 PBAC Meeting).
Proposed vaccine cost per dose	$[redacted]	
Vaccine administration	GP administration: First dose $7.84 based on MBS item 3 ($19.60) * 50% * Second dose $15.68 based on MBS item 3 (19.60) Pharmacy administration: $20.05 'Other' administration: no cost	GP administration 82.8%, pharmacy administration 9.4% and administration by 'other' 7.8%. The submission assumed that administration of the first dose is relatively easy to combine with another medical intervention when administered in a GP setting (e.g., concomitant administration with influenza vaccination; or routine GP consultation involving the discussion of other health conditions, Therefore, the cost of administration of the first dose was assumed to be 50% of GP consultation. The ESC considered the assumptions regarding how RZV would be administered were poorly supported in the submission and costs are therefore likely to be inaccurate and may be underestimated.

Source: Compiled during the evaluation from Sections 4.1-4.5, pp 325-349

ABS = Australian Bureau of Statistics; AIR = Australian Immunisation Register; ATAGI = Australian Technical Advisory Group on Immunisation; GP = general practitioner; IC = immunocompromised; MBS = Medicare Benefits Schedule; OLS = ordinary least squares; PBAC = Pharmaceutical Benefits Advisory Committee; RZV = recombinant zoster vaccine, Shingrix®; UK, United Kingdom

Table 17 estimates the total financial implications for the NIP of listing of RZV for non-Indigenous adults aged 60-64.

Table 17: Estimated use and financial implications

	2026 (Y1)	2027 (Y2)	2028 (Y3)	2029 (Y4)	2030 (Y5)	2031 (Y6)	Total
Total doses administered (new program)	[redacted]1	[redacted]2	[redacted]3	[redacted]3	[redacted]4	[redacted]4	[redacted]5
Total doses administered (existing program)	[redacted]6	[redacted]7	[redacted]8	[redacted]8	[redacted]4	[redacted]4	[redacted]9
Net total doses administered	[redacted]1	[redacted]4	[redacted]7	[redacted]10	[redacted]11	[redacted]12	[redacted]10
Net NIP cost	$[redacted]13	$[redacted]14	$[redacted]15	$[redacted]16	$[redacted]16	$[redacted]16	$[redacted]17

	2026 (Y1)	2027 (Y2)	2028 (Y3)	2029 (Y4)	2030 (Y5)	2031 (Y6)	Total
Impact on other medications (PBS/RPBS)	-$ [redacted][28]	-$ [redacted][28]	-$ [redacted][28]	-$ [redacted][28]	-$ [redacted][28]	-$ [redacted][28]	-$ [redacted][28]
Net cost to MBS	$ [redacted][18]	$ [redacted][18]	$ [redacted][18]	$ [redacted][18]	$ [redacted][18]	-$ [redacted][28]	$ [redacted][16]
Net cost to State, Territories and Commonwealth[a]	-$ [redacted][28]	-$ [redacted][28]	-$ [redacted][28]	-$ [redacted][28]	-$ [redacted][28]	-$ [redacted][28]	-$ [redacted][28]
Net cost to Health System[a]	$ [redacted][13]	$ [redacted][14]	$ [redacted][19]	$ [redacted][16]	$ [redacted][18]	$ [redacted][18]	$ [redacted][17]
Updated in PSCR							
Total doses administered 60-64	[redacted][2]	[redacted][8]	[redacted][7]	[redacted][7]	[redacted][7]	[redacted][7]	[redacted][20]
Total doses administered (existing program)	[redacted][6]	[redacted][12]	[redacted][9]	[redacted][10]	[redacted][10]	[redacted][7]	[redacted][21]
Net total doses administered	[redacted][2]	[redacted][7]	[redacted][10]	[redacted][10]	[redacted][22]	[redacted][23]	[redacted][9]
Net NIP cost	$ [redacted][24]	$ [redacted][25]	$ [redacted][26]	$ [redacted][16]	$ [redacted][18]	$ [redacted][18]	$ [redacted][13]
Impact on other medications (PBS/RPBS)	-$ [redacted][27]	-$ [redacted][28]	-$ [redacted][28]	-$ [redacted][28]	-$ [redacted][28]	-$ [redacted][28]	-$ [redacted][28]
Net cost to MBS	$ [redacted][18]	$ [redacted][18]	$ [redacted][18]	$ [redacted][18]	$ [redacted][18]	$ [redacted][18]	$ [redacted][16]
Net cost to State, Territories and Commonwealth[a]	-$ [redacted][28]	-$ [redacted][28]	-$ [redacted][28]	-$ [redacted][28]	-$ [redacted][28]	-$ [redacted][28]	-$ [redacted][28]
Net cost to Health System	$ [redacted][27]	$ [redacted][25]	$ [redacted][26]	$ [redacted][18]	$ [redacted][18]	$ [redacted][18]	$ [redacted][13]

Source: Tables 4-3 & 4-25, pp352 of the submission

MBS = Medicare Benefits Schedule; PBS = Pharmaceutical Benefits Schedule; RPBS = Repatriation Pharmaceutical Benefits Scheme

a Includes costs/ savings for emergency visits, hospitalisations and pharmacy vaccination

The redacted values correspond to the following ranges:

[1] *900,000 to < 1,000,000*
[2] *600,000 to < 700,000*
[3] *500,000 to < 600,000*
[4] *400,000 to < 500,000*
[5] *3,000,000 to < 4,000,000*
[6] *< 500*
[7] *200,000 to < 300,000*
[8] *300,000 to < 400,000*
[9] *1,000,000 to < 2,000,000*
[10] *100,000 to < 200,000*
[11] *80,000 to < 90,000*
[12] *70,000 to < 80,000*
[13] *$100 million to < $200 million*
[14] *$60 million to < $70 million*
[15] *$30 million to < $40 million*
[16] *$10 million to < $20 million*
[17] *$200 million to < $300 million*
[18] *$0 to < $10 million*
[19] *$20 million to < $30 million*
[20] *2,000,000 to < 3,000,000*
[21] *700,000 to < 800,000*
[22] *60,000 to < 70,000*
[23] *50,000 to < 60,000*

[24] *$80 million to < $90 million*
[25] *$40 million to < $50 million*
[26] *$20 million to < $30 million*
[27] *$90 million to < $100 million*
[28] *net cost saving*

6.70 The total cost to the NIP of listing RZV for non-Indigenous adults aged 60-64 was estimated to be $120 million to < $130 million in Year 1 decreasing to $10 million to < $20 million in Year 6, and a total cost of $200 million to 300 million. These estimates are uncertain for several reasons:

- The absolute growth in uptake rate for non-Indigenous adults aged ≥65 was predicted for years 1-2 based on extrapolation using ordinary least squares regression of AIR data since NIP listing November 2023 (39.2% in May 2025 extrapolated to 40.4% for 1st Jan 2026) for over 65s. For years 3-6 a relative growth rate assumption of 50% was applied which the submission reported aligned with UK data on HZ vaccine coverage for over 70s by the end of June 2023 (UK Health Security Agency, 2024b). ATAGI considered that UK data would likely overestimate vaccine uptake as it is from an older cohort who are likely to have more contact with primary providers and for whom vaccination is likely to be seen as a higher priority, and furthermore the UK health system is different to Australia's (ATAGI pre-PBAC advice, April 2025). The PSCR provided revised financials using AIR data to 2 September 2025 to estimate uptake in individuals ≥ 65 YOA (based on an exponential model fitted to monthly data). The coverage for individuals 60-64 YOA was assumed to be the same as predicted for ≥65 YOA with 1) a 21.6% reduction to account for lower uptake in the 65-69 vs ≥65 YOA cohort (42.5% vs 54.2%, based on September 2025 data), and 2) another 20% reduction to account for predicted lower coverage in the 60-64 vs 65-69 YOA cohort.
- Vaccine uptake rates in non-Indigenous adults aged 60-64 were assumed to be 15% lower than those aged ≥65. This is higher that the ATAGI pre-PBAC advice which reported that a base case which applied a 20% reduction relative to ≥65 (with sensitivity analyses at 15% and 20%) was reasonable (ATAGI pre-PBAC advice, April 2025). The PSCR provided updated financials assuming a 20% relative reduction.
- Second dose compliance was assumed to be 82% in both the 60-64 YOA cohort and those ≥65. This rate was based on the midpoint of 12-month series completion rates reported across post-marketing studies in Canada and the USA The PSCR provided updated financials assuming second dose compliance of 80.3% in the 60 to 64 YOA cohort.

6.71 The PSCR provided revised financials that estimated the net cost to the NIP of listing RZV for non-Indigenous adults aged 60-64 was estimated to be $80 million to < $90 million in Year 1 decreasing to $0 to < $10 million in Year 6, and a total cost of $100 million to < $200 million.

6.72 The submission anticipated a reduction in the use of medications used to treat HZ, PHN and non-PHN complications which would result in a total PBS/RPBS saving of$0 to < $10 million. These estimates are reliant on outputs from the economic model and it is likely that the cost-savings to the PBS/RPBS have been overestimated.

6.73 The total net cost to the MBS was estimated at $10 million to < $20 million in Year 1 ($0 to < $10 million in PSCR) decreasing to $0 to < $10 million in Year 6 ($0 to < $10 million in PSCR). Increases in costs to the MBS were driven by administration costs for RZV and vaccine associated adverse events. Cost offsets to the MBS were driven by reduced incidence of HZ, PHN and non-PHN complications. These cost offsets were likely overestimated as they were based on outputs from the economic model.

Quality Use of Vaccines

6.74 The submission indicated ongoing educational activities for RZV, targeted at immunisation providers and other healthcare professionals, which support optimal RZV administration and 2-dose schedule adherence. The submission further indicated a commitment to working closely with various implementation partners, vaccine providers and consumer groups in Australia to help ensure quality use of medicines (QUM) principles are upheld according to The National Strategy for QUM.

6.75 The priority of vaccinating different populations was discussed at the ESC meeting. It was noted that (i) increasing uptake in individuals aged over 65 years of age and (ii) improving access for individuals over 18 years of age with a broader range of conditions that have a moderate risk of HZ infection may be of a higher priority than broadening access to individuals 60 to 64 years of age.

For more detail on PBAC's view, see section 7 PBAC outcome.

7 PBAC Outcome

7.1 The PBAC did not recommend a change to the circumstances under which recombinant zoster vaccine (RZV) is made available as a designated vaccine for the purposes of the National Health Act 1953. The PBAC considered vaccinating individuals at 60 years of age would result in a reduction in protection in older individuals when the prevalence of herpes zoster (HZ) and post-herpetic neuralgia (PHN) was higher and morbidity could be more severe. The PBAC considered the incremental cost effectiveness ratio presented in the submission was high and highly uncertain. The PBAC noted assumptions regarding waning of vaccine efficacy (VE) over time were uncertain (particularly after around 8 to 10 years) and this was a key driver of the economic model. The PBAC noted the financial cost of lowering the age of vaccination was high.

7.2 The PBAC considered that the primary reason for this outcome was the economic evaluation.

7.3 The PBAC noted the consumer comments were supportive of expanding the access to RZV on the NIP. Comments noted the potential long-term negative health and quality

of life implications of HZ and PHN. The PBAC noted some comments were not specifically related to expanding access to individuals from 60 years of age but expanding the definition of the immunocompromised population who can currently access RZV on the NIP.

7.4 The PBAC noted the comments from Crohn's and Colitis Australia regarding the importance of access for individuals on (or about to commence) therapies that result in immunosuppression (such as some inflammatory bowel disease treatments). The PBAC noted that the Australian Immunisation Handbook recommends that *"When feasible, all indicated vaccines should be given ≥4 weeks before starting immunosuppressive medications"* for patients with secondary immunodeficiency due to medical therapies.

7.5 The PBAC noted the submission nominated no vaccination in individuals 60 to 64 years of age as the comparator and considered this was appropriate, in the context that the economic analysis and financial estimates were based on a comparison of vaccination at 60 years of age to vaccination at 65 years of age.

7.6 The PBAC noted the submission was based on studies it had previously considered, two head-to-head randomised studies comparing RZV to placebo (ZOE-50 and ZOE-70) and a long term follow up study (ZOSTER-049). The ZOE-50 and ZOE-70 data remained unchanged from the previous submissions. The PBAC noted additional follow up was provided for the ZOSTER-049 study (median of 11.5 years post-vaccination in this submission, compared to mean of 9.6 years post-vaccination considered previously). The PBAC noted the ZOSTER-049 study used historical controls derived from the placebo arms of the ZOE-50 and ZOE-70 studies. The PBAC noted there was a decline in vaccine efficacy against HZ (VE_{HZ}) over time in the overall cohort with increasing variability, with VE_{HZ} of 73.68% (95%CI: 52.89, 86.16) at Year 9 and 71.70% (95%CI: 49.03, 85.18) at Year 10. The PBAC noted the VE_{HZ} at Year 11 increased but maintained that, overall, the data indicate a decline in VE_{HZ} over time. The PBAC noted the safety data remained essentially unchanged from the previous submissions. The PBAC considered the claim that RZV is superior in terms of effectiveness and inferior in terms of safety compared to no vaccination in individuals 60 to 64 years of age was reasonable.

7.7 Despite the concerns regarding the ZOSTER-049 study (see paragraph 6.13), the PBAC considered it provided reasonable evidence that RZV resulted in durable protection against HZ and PHN for up to approximately 8 to 10 years; however, the PBAC considered there were some uncertainties regarding the long term estimates of vaccine efficacy. The PBAC considered it was likely protection would reduce over time (see Figure 1) and vaccinating individuals at 60 years of age (compared to 65 years of age) would result in a reduction in protection in older individuals when the prevalence of HZ and PHN was higher and morbidity is generally more severe.

7.8 The PBAC noted the base case ICER (applying a 5% discount rate) was $15,000 to < $25,000 per quality adjusted life year (QALY). The PBAC noted this was higher than the

ICER recommended for individuals vaccinated at 65 years of age ($5,000 to < $15,000to $15,000 to < $25,000 per QALY depending on the source of HZ incidence, paragraph 5.7, RZV PSD, July 2023 PBAC meeting).

7.9 The PBAC noted the economic model was sensitive to assumptions regarding long term VE and how quickly VE would wane. The PBAC noted the model assumed VE_{HZ} of more than 50% at 20 years post-vaccination. The PBAC noted the economic model applied different waning rates to individuals < 70 years of age and ≥ 70 years of age (see paragraph 6.51) which resulted in VE waning faster after 10 years for individuals vaccinated at 60 years of age compared to after 5 years for individual vaccinated at 65 years of age. The PBAC noted applying a constant annual waning of 1.2% to all individuals decreased the ICER by [redacted]% and applying a constant annual waning of 2.1% (i.e., a difference of less than one percentage point) increased the ICER by [redacted]%. Additionally, the PBAC noted the ESC considered it remained uncertain if a linear waning model was reasonable and the PBAC noted it was not possible to assess the impact on cost-effectiveness of assuming non-linear waning.

7.10 Noting concerns regarding the model assumptions (as outlined in paragraph 7.9), the PBAC noted the economic model predicted vaccinating 1 million individuals at 60 years of age rather than 65 years of age would result in 48,459 fewer HZ cases in individuals aged 60 to 64 years. However, this is offset by an additional 14,053 HZ cases in individuals aged 65 to 100 years, including an additional 4,027 HZ cases in individuals aged ≥ 80 years. The PBAC considered the more serious sequelae of HZ that can be experienced by older cohorts may not have been adequately captured in the model given the QALY loss per HZ case in individuals over 80 years of age was only marginally higher than the QALY loss in individuals 60 to 69 years of age (see paragraph 6.53).

7.11 The PBAC noted the incremental cost of lowering the age of vaccination from 65 to 60 years of age was high ($[redacted] over 6 years in the PSCR).

7.12 The PBAC noted that this submission is not eligible for an independent review as independent review is only relevant to requests for PBS listing.

Outcome:

Not recommended.

8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available

through the PBS. The PBAC welcomes applications containing new information at any time.

9 Sponsor's Comment

GSK acknowledges the PBAC's decision regarding Shingrix for adults aged 60–64 years. We remain committed to ensuring Australians have access to effective prevention against shingles and its complications. Herpes zoster continues to impose a significant impact on health, productivity and quality-of-life burden, and vaccination is the most effective way to reduce this risk. We look forward to continuing to work with the Government to improve coverage in the existing populations, while also seeking to expand eligibility for Shingrix vaccination on the NIP to populations who remain at risk of shingles.