

## 7.11 VARICELLA ZOSTER VIRUS RECOMBINANT VACCINE, Injection [1 vial] & adjuvant substance diluent [0.5 mL vial], Shingrix®, GlaxoSmithKline Australia Pty Ltd.

### 1 Purpose

- 1.1 The early re-entry resubmission requested a National Immunisation Program (NIP) listing for varicella zoster virus recombinant vaccine (RZV) for the prevention of herpes zoster (HZ) and post-herpetic neuralgia (PHN) for non-Indigenous individuals aged 65 to 69 years and ≥ 71 years.

**Table 1: Key components of the clinical issue addressed by the resubmission**

Component	Description
Population	Perpetual catch-up for individuals aged ≥ 71 years (primary vaccination for individuals aged 70 years was recommended at the March 2023 PBAC meeting) OR Primary program for individuals aged 65 years and a catch-up program for individuals aged ≥ 66 years. (See paragraph 3.1)
Intervention	Recombinant Varicella Zoster Virus glycoprotein E antigen (AS01 <sub>B</sub> adjuvanted) vaccine (RZV) (2-doses 2 to 6 months apart)*
Comparator	No vaccine
Outcomes	Efficacy: Cases of HZ, cases of PHN, and HZ-associated complications. Safety: Solicited local and general AEs, unsolicited AEs, and SAEs.
Clinical claim	RZV versus no vaccine: superior efficacy and 'slightly' inferior safety.

Source: Based on Table 1-2 of the resubmission

AE = adverse event; HZ = herpes zoster; PHN = post-herpetic neuralgia; SAE = serious adverse event.

\* For adults who are immunodeficient, immunosuppressed or likely to become immunosuppressed due to known disease or therapy, and who would benefit from a shorter vaccination schedule, the second dose can be given 1 to 2 months after the initial dose

### 2 Background

- 2.1 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 conditions at high risk of HZ infection. Conditions with a high risk of HZ infection included haemopoietic stem cell transplant, solid organ transplant, haematological malignancy and advanced or untreated human immunodeficiency virus (HIV). Funding for the inclusion of RZV on the NIP for this population was included in the 2023-24 Budget and it will be included on the NIP from 1 November 2023.
- 2.2 The PBAC considered there was likely to be a broader population of immunocompromised individuals aged ≥ 18 years at increased risk of HZ for whom RVZ was similarly cost effective to the populations recommended in paragraph 2.1,

but this population had not yet been clearly defined. The PBAC deferred a decision regarding this population to seek further ATAGI advice. ATAGI advice for this population is expected on the 27 September 2023.

2.3 The PBAC did not recommend RZV for non-Indigenous individuals aged 65 to 69 years and ≥ 71 years. The early re-entry resubmission is for this population.

2.4 This resubmission addressed the issues raised by the PBAC; see table below.

**Table 2: Summary of key matters to be addressed**

Matter of concern	Response
The PBAC considered a price reduction would be required for RZV to be cost-effective for these populations, noting that they were of lower clinical priority and represented a high volume of doses (5,000,000 to < 6,000,000 doses over 6 years with an associated cost of \$900 million to < \$ 1 billion). In the context of the total cost, the PBAC considered the extent of uncertainty regarding the cost-effectiveness of RZV to be too high. [paragraph 7.21, RZV PSD, March 2023 PBAC meeting]	Cost per dose reduced from \$█ to \$█ or \$█ depending on the populations recommended and timing of listing on the NIP.
The ICER was sensitive to the incidence of HZ, VE estimates, assumptions regarding long-term waning of efficacy, and the assumed QALY loss per HZ and PHN event. The PBAC maintained [its previous] advice and considered that any resubmission should present additional cost effectiveness analyses including univariate and multivariate analyses addressing the issues [identified above]. [paragraphs 7.21 and 7.24, RZV PSD, March 2023 PBAC meeting]	No univariate or multivariate analyses were provided. Rather, the resubmission stated that any uncertainty could be addressed with a lower base case ICER. The base case ICERs using a reduced cost per dose ranged from \$█ <sup>1</sup> /QALY to \$█ <sup>1</sup> /QALY, depending on the population and scenario (compared to \$█ <sup>2</sup> /QALY in the previous submission).
The PBAC considered the estimated financial cost of listing RZV on the NIP for non-Indigenous individuals aged 65 to 69 years and ≥ 71 years could reliably be determined using the estimates model provided in the resubmission. The PBAC noted in any resubmission individuals previously vaccinated with 2 doses of RZV and individuals who have received ZVL in the previous 5 years should be removed from the estimates. The PBAC noted the ATAGI post-submission advice indicated the proportion of the population that has previously received ZVL was higher than assumed in the resubmission. [paragraph 7.25, RZV PSD, March 2023 PBAC meeting]	The resubmission: <ul style="list-style-type: none"> <li>- excluded individuals previously vaccinated with 2 doses of RZV and individuals who have received ZVL in the previous 5 years.</li> <li>- amended the proportion of individuals that had previously received ZVL as requested.</li> <li>- amended the cumulative uptake rates to a maximum of 65% for the primary vaccination program of individuals aged 65 years (to be consistent with the uptake rates in other age cohorts, as discussed in Table 17 of the RZV March 2023 PBAC minutes).</li> </ul>

Source: 7.04 RZV PBAC minutes, March 2023 PBAC meeting. Constructed during the preparation of the submission overview.

HZ = herpes zoster; ICER = incremental cost-effectiveness ratio; NIP = National Immunisation Program; PHN = post-herpetic neuralgia; QALY = quality adjusted life year; RVZ = recombinant zoster vaccine; ZVL = zoster vaccine live; PSD = Public Summary Document

The redacted values correspond to the following ranges:

<sup>1</sup> \$5,000 to < \$15,000

<sup>2</sup> \$15,000 to < \$25,000

For more detail on PBAC’s view, see section 5 PBAC outcome.

### 3 Requested listing

Name, Restriction, Manner of administration and form	Price requested by sponsor	Proprietary Name and Manufacturer	
Recombinant Varicella Zoster Virus Glycoprotein E Antigen (AS01 <sub>B</sub> Adjuvanted) Vaccine; powder and suspension for injection, 0.5 mL; Shingrix® GSK	\$■■■/ \$■■■	Shingrix®	GSK

- 3.1 In March 2023, the PBAC recommended RZV be included on the NIP for the primary vaccination of individuals aged 70 years. The resubmission requested NIP listing for RZV for individuals aged 65 to 69 years and ≥ 71 years. Should the PBAC recommend NIP listing for individuals aged ≥ 71 years only, this could be implemented as a catch-up program (with primary vaccination aged 70 years). Should the PBAC recommend NIP listing for individuals aged 65 to 69 years and ≥ 71 years, this could be implemented as a primary program for individuals aged 65 years and a catch-up program for individuals aged ≥ 66 years. The pre-PBAC response proposed the following wording for the determination, depending on the proposed non-Indigenous program under consideration: ‘Vaccine may be provided to a person who is at least 65 years of age as of [date of inclusion on the NIP] OR at least 70 years of age as of [date of inclusion on the NIP].’ The PBAC noted the proposed wording does not exclude individuals previously vaccinated with RZV or individuals previously vaccinated with Zoster vaccine live (ZVL) in the previous 5 years.
- 3.2 ZVL was listed on the NIP for individuals aged 70 years with a time limited catch-up program for individuals aged 71-79 years. The proposed listing for RZV expands the catch-up program to an older cohort (includes those aged ≥ 80 years) and reduces the age for the primary vaccination from 70 years to 65 years. The pre-PBAC response noted the recommendation of an NIP listing of ZVL for adults 70-79 YOA was based on reduced initial vaccine efficacy (VE) in adults ≥80 YOA and reduced cost-effectiveness in adults <70 YOA, with rapidly waning efficacy after vaccination. The pre-PBAC response argued RZV has demonstrated superior VE compared with ZVL, regardless of age, where VE<sub>HZ</sub> was 97.2% in adults aged ≥50 years (ZOE-50 trial) and was 91.3% and 91.4% in adults aged ≥70 and ≥80 years, respectively (pooled ZOE-50/-70 trials). It was further argued that RZV VE<sub>HZ</sub> was highly durable, with overall VE<sub>HZ</sub> of 89% (95% CI, 85.6%-91.3%), 1 month post-dose 2 in ZOE-50/70 to a mean of 9.6 (±0.3) years post-vaccination in the ZOE-50/-70 trials (ZOSTER-049 Y4 Interim Analysis [IA]), and was consistently robust in post-hoc analyses in frail or pre-frail adults (>90%), adults with ≥1 potential immune related disorders (pIMD) (90.5%), and adults with chronic medical conditions (≥84.5%).

*For more detail on PBAC’s view, see section 5 PBAC outcome.*

## 4 Consideration of the evidence

### ***Sponsor hearing***

4.1 There was no hearing for this item.

### ***Consumer comments***

- 4.2 The PBAC noted and welcomed the input from health care professionals (13) and organisations (2) via the Consumer Comments facility on the PBS website. The comments from health care professionals noted that RZV reduced the risk of HZ infection and the associated morbidity and mortality and that RZV provided higher and longer efficacy compared to ZVL. The comments noted that RZV is safer compared with ZVL and noted the evidence that it is safe and effective among individuals undergoing immunosuppressive treatment. The input also noted the impact of HZ infection on quality of life and described the improvements RZV would have on their daily lives. The comments noted equity issues associated with the current high cost of RZV and that many individuals were unable to afford the vaccine privately.
- 4.3 The PBAC noted the input received from Gastroenterological Society of Australia (GESA) and Crohn's and Colitis Australia regarding the importance of including RZV on the NIP for individuals who have immune mediated inflammatory diseases (IMIDs) as they are at increased risk of HZ due to the immunosuppressant medications they may be receiving. The GESA and Crohn's and Colitis Australia expressed concern that due to the high cost of RZV many individuals with IMID are currently unable to access the vaccine, placing them at increased risk of an infection and the morbidity and mortality associated with HZ infection. Pain Australia noted the significant impact of HZ infection on an individual's quality of life and supported the extension of the NIP listing of RZV and considered that RZV should be made available to all individuals aged 50 years and older. Pain Australia noted that individuals aged 50 years and older were more likely to suffer from chronic conditions making them more vulnerable to preventable diseases, such as HZ, and were at greater risk of experiencing severe illness and mortality from infection.

### ***Clinical evidence***

- 4.4 No new clinical evidence was provided in the resubmission.
- 4.5 The PBAC previously noted the vaccine efficacy against HZ ( $VE_{HZ}$ ) for individuals who received two doses of RZV was high (90% to 97%) and while  $VE_{HZ}$  appeared to be reducing over time, it remained high (84%) after 8 years (paragraph 7.9, RZV Public Summary Document (PSD), March 2023 PBAC meeting).

### ***Clinical claim***

- 4.6 The PBAC reaffirmed its March 2023 advice that the clinical claim that RZV is superior in terms of effectiveness compared with placebo and slightly inferior in terms of safety

compared to placebo for the proposed NIP populations was reasonable (paragraph 7.8, RZV PSD, March 2023 PBAC meeting).

### ***Economic analysis***

4.7 As an early re-entry resubmission, the economic analysis was not independently evaluated.

4.8 In March 2023, the PBAC considered the extent of uncertainty regarding the cost-effectiveness of RZV for non-Indigenous individuals aged 65 to 69 years and  $\geq 71$  years to be too high. At the March 2023 meeting, the PBAC maintained its advice from the November 2018 consideration that given the large opportunity cost of including RZV on the NIP for this population, more conservative cost-effectiveness analyses were required. The PBAC advised that any resubmission should present additional cost effectiveness analyses including univariate and multivariate analyses addressing the issues outlined below:

- Incidence of HZ: The PBAC previously noted the ATAGI post-submission advice that the best estimate of incidence was a pooled estimate using data from MacIntyre 2015, Qian 2021 and Lin 2022; however, this was not included in the resubmission considered in March 2023. The PBAC previously noted the incremental cost-effectiveness ratio (ICER) for vaccinating non-Indigenous adults  $\geq 65$  years increased from \$15,000 to  $< \$25,000$ /quality adjusted life year (QALY) to \$25,000 to  $< \$35,000$ /QALY using pooled data from MacIntyre 2015 and Qian 2021 and to \$35,000 to  $< \$45,000$ /QALY using Qian 2021 alone.
- VE estimates: The PBAC previously noted the ATAGI post-submission advice that the vaccine effectiveness for two doses from Izurieta 2021 (a large observational study) could be used in sensitivity analyses, and that use of this estimate increased the ICER for vaccinating non-Indigenous adults  $\geq 65$  years from \$15,000 to  $< \$25,000$ /QALY to \$35,000 to  $< \$45,000$ /QALY. The pre-PBAC response noted that the post-submission ATAGI advice also stated that the 'inclusion of the Izurieta 2021 data was to provide more information regarding the evidence of the one-dose vaccine effectiveness of Shingrix' and that the 'ATAGI agree that using the vaccine efficacy data from the clinical trials is appropriate'. For this reason, the sponsor considered that a scenario analysis adopting both single-dose and two-dose VE estimates from Izurieta 2021 to be inappropriate. The pre-PBAC response argued that the study design of Izurieta 2021 resulted in the underestimation of the RZV VE due to differences in outcome specificity and confounding due to healthcare seeking behaviour.
- Long term waning of efficacy: The PBAC previously noted the ICER for vaccinating non-Indigenous adults  $\geq 65$  years increased from \$15,000 to  $< \$25,000$ /QALY to \$25,000 to  $< \$35,000$ /QALY if an annual waning rate of 5.4% was assumed from 10 years after vaccination, which was higher than the annual waning rate of 1.5% for adults  $<70$  YOA and 2.3% for adults  $\geq 70$  YOA applied in the base-case of the

economic model. The PBAC also noted the waning assumptions become more critical when vaccinating a younger cohort.

- QALY loss per HZ and PHN event: The ICER was sensitive to the assumed QALY loss per HZ and PHN event and the ESC considered the QALY loss per case of HZ and PHN were overestimated given the trial data demonstrated attenuation of disease impact over the period of HZ. The PBAC previously noted the ICER increased to \$25,000 to < \$35,000/QALY when the lower 95% confidence intervals were used to inform the QALY loss per event. The pre-PBAC response reiterated that the in-trial disutilities for HZ episodes underestimated the quality of life (QoL) burden per case of HZ due to earlier initiation of antiviral therapy compared with clinical practice. The pre-PBAC response argued that HZ episodes persist beyond a 28-day period in the age cohorts most relevant to the proposed NIP populations (Curran, 2019)<sup>1</sup>, and based on the ZOE-50/-70 Zoster Brief Pain Inventory (ZBPI) data, 22.4% (ZOE-50, ≥50 YOA) and 32.3% (pooled ZOE-50/-70, aged ≥ 70 years) of patients in the HZ ZBPI evaluable subgroups had a ZBPI worst pain score of ≥ 3 at Day 28. The pre-PBAC response argued that the base case disutility estimates per HZ case were conservative, as they did not incorporate differential QALY losses for breakthrough HZ cases in RZV-vaccinated subjects relative to unvaccinated subjects and noted that a meta-analysis of the ZOE-50/-70 and ZOSTER-002 trials estimated a mean difference in QALY losses for HZ cases in vaccinated vs unvaccinated subjects of 0.00722 (GSK, 2022; data on file).

- 4.9 The resubmission stated that the remaining issues in the non-Indigenous population aged 65 to 69 years and ≥ 71 years appeared to be related to opportunity cost and cost-effectiveness, which may be resolvable with a price reduction rather than re-evaluation of economic model inputs. The resubmission maintained that the economic model inputs were reasonable and robust, and that incorporating more conservative and less robust assumptions would strongly bias against RZV.
- 4.10 The economic model provided with the resubmission was the same as the model considered in March 2023 with two changes (i) reduced cost per dose and (ii) separate cohorts for individuals aged 71 to 79 years and ≥ 71 years (to account for individuals aged 70 years being recommended in March 2023). The economic model also included a separate cohort of individuals aged ≥ 80 years.
- 4.11 The resubmission considered the two requested age cohorts separately (individuals aged 65 to 69 years and ≥ 71 years) and proposed three scenarios with different costs per dose as summarised in Table 3. Scenario C assumed both age cohorts were

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<sup>1</sup> Curran D, Oostvogels L, Heineman T, Matthews S, McElhaney J, McNeil S, Diez-Domingo J, Lal H, Andrews C, Athan E, Berglund J, Campora L, de Looze F, Korhonen T, Leung E, Levin M, Volpi A, Johnson RW; ZOE-50/70 Study Group. Quality of Life Impact of an Adjuvanted Recombinant Zoster Vaccine in Adults Aged 50 Years and Older. *J Gerontol A Biol Sci Med Sci*. 2019 Jul 12;74(8):1231-1238.

recommended for inclusion on the NIP (as for Scenario B) with listing for individuals aged 65 to 69 years implemented later (assumed one year later in the resubmission) than the listing for individuals aged ≥ 71 years. The timing of inclusion on the NIP is not a matter for the PBAC.

**Table 3: Scenarios proposed for consideration**

Scenario	Population	Cost per dose
A.	Individuals aged ≥ 71 years	\$ [redacted]
B.	Individuals aged 65 to 69 years and ≥ 71 years	\$ [redacted]
C.	Individuals aged 65 to 69 years and ≥ 71 years with the younger age group implemented at a later date than the older age group	\$ [redacted] for 65 to 69 years \$ [redacted] for ≥ 71 years

Source: based on information provided in Table 1-1 of resubmission

4.12 A summary of the cost per dose, number needed to vaccinate (NNV), incremental costs and benefits and incremental cost per QALY gained for each of the relevant age cohorts is provided in Table 4. Although the ICERs are reasonably consistent across the age cohorts as outlined below the ICERs are sensitive to different assumptions.

**Table 4: Summary of modelled outcomes for each age cohort**

Result	Aged 65-69 years	Aged ≥71 years	Aged 71-79 years	Aged ≥80 years
Cost per dose of RSV	\$ [redacted]	\$ [redacted]	\$ [redacted]	\$ [redacted]
NNV to avoid one case of HZ	5	7	6	8
NNV to avoid one case of PHN	23	27	25	30
Incremental costs per 1,000,000 vaccinated individuals	\$ [redacted]	\$ [redacted]	\$ [redacted]	\$ [redacted]
Incremental QALYs per 1,000,000 vaccinated individuals	8,615	8,469	8,627	8,215
Incremental cost per QALY gained	\$ <sup>1</sup> [redacted]	\$ <sup>1</sup> (\$ [redacted] <sup>1</sup> )	\$ <sup>2</sup> (\$ [redacted] <sup>1</sup> )	\$ <sup>1</sup> (\$ [redacted] <sup>1</sup> )

Source: Table 3-3 in resubmission

HZ = herpes zoster; NNV = number needed to vaccinate; PHN = post-herpetic neuralgia; QALY = quality-adjusted life year; RZV = recombinant zoster vaccine

The redacted values correspond to the following ranges:

<sup>1</sup> \$5,000 to < \$15,000

<sup>2</sup> \$15,000 to < \$25,000

**Scenario A: Individuals aged ≥ 71 years (catch-up program), cost per dose of \$ [redacted]**

4.13 The base case ICER for individuals aged ≥ 71 years with a cost per dose of \$ [redacted] was \$5,000 to < \$15,000/QALY applying a 5% discount rate to costs and outcomes and \$5,000 to < \$15,000/QALY applying a 3.5% discount rate. The resubmission did not present sensitivity analyses. Sensitivity analyses for the scenarios presented in the March 2023 PBAC PSD and noted in paragraph 4.7 above have been replicated in Table 5. Results for individuals aged 71 to 79 and ≥ 80 years are also presented in Table 5.

Table 5: Results of sensitivity analyses for individuals aged ≥ 71 years (cost per dose of \$ [redacted])

	Age cohort				
	≥ 71 years		71 to 79 years	≥ 80 years	
Analyses (per 1,000,000 individuals vaccinated)	Incremental cost (\$)	Incremental QALY	ICER (% change from base case)	ICER (% change from base case)	ICER (% change from base case)
<b>Base case</b>	[redacted]	8,469	[redacted] <sup>1</sup>	\$ [redacted] <sup>2</sup>	\$ [redacted] <sup>1</sup>
Discount rate (base case 5% costs and outcomes)					
3.5% costs and outcomes	[redacted]	9,227	[redacted] <sup>1</sup> (-21%)	[redacted] <sup>1</sup> (-22%)	[redacted] <sup>1</sup> (-18%)
HZ Incidence (base case MacIntyre 2015)					
MacIntyre 2015 + Qian 2021 [using a cost per dose of \$ [redacted]]	[redacted]	7,321 [7,615]	[redacted] <sup>2</sup> (+41%)	[redacted] <sup>2</sup> (+31%)	[redacted] <sup>2</sup> (+64%)
Qian 2021	[redacted]	6,154	[redacted] <sup>3</sup> (+98%)	[redacted] <sup>3</sup> (+71%)	[redacted] <sup>3</sup> (+163%)
MacIntyre 2015 but assuming same HZ incidence in individuals aged 71 to 79 years and ≥ 80 years	[redacted]	7,003	[redacted] <sup>2</sup> (+53%)	[redacted] <sup>2</sup> (+63%)	[redacted] <sup>3</sup> (+119%)
Vaccine efficacy (base case ZOE-50 and ZOE-70)					
Using effectiveness data from Izureita 2021	[redacted]	5,656	[redacted] <sup>3</sup> (+125%)	[redacted] <sup>4</sup> (+119%)	[redacted] <sup>3</sup> (+138%)
RZV waning (base case ZOE-50, ZOE-70, ZOSTER-49)					
Alternate waning rate of 5.4% beginning at 10 years	[redacted]	7,906	[redacted] <sup>2</sup> (+19%)	[redacted] <sup>2</sup> (+26%)	[redacted] <sup>1</sup> (+7%)
QALY loss for HZ & HZ with PHN (base case Gater 2014, Serpell 2014, Curran 2017)					
Lower 95% confidence interval	[redacted]	5,437	[redacted] <sup>2</sup> (+56%)	[redacted] <sup>3</sup> (+56%)	[redacted] <sup>2</sup> (+55%)

Source: Table 3-3, Table 3-4, 7b. RZV ZONA CEA 71-79, 71+ YOA.xls provided with resubmission. Constructed during the development of the submission overview.

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

The redacted values correspond to the following ranges:

<sup>1</sup> \$5,000 to < \$15,000

<sup>2</sup> \$15,000 to < \$25,000

<sup>3</sup> \$25,000 to < \$35,000

<sup>4</sup> \$35,000 to < \$45,000

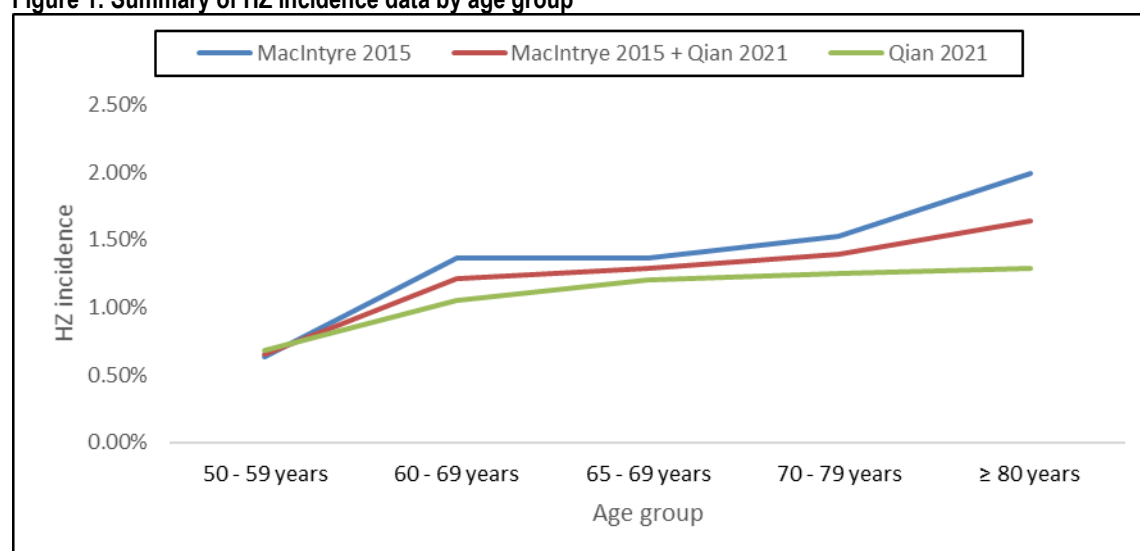
4.14 With a cost per dose of \$ [redacted] the ICERs ranged from \$15,000 to < \$25,000/QALY for the scenario with an alternative vaccine efficacy waning assumption to \$25,000 to < \$35,000/QALY for the scenario with vaccine efficacy based on vaccine effectiveness in Izurieta 2021.

4.15 The resubmission noted that one of the main suggested amendments to the economic model was to utilise a lower HZ incidence rate as determined through pooling of 2 less robust studies (Lin 2022 and Qian 2021) which are considered to underestimate HZ incidence with a study that could possibly overestimate HZ incidence (MacIntyre 2015). The resubmission stated that reducing HZ incidence without amending PHN risk post HZ will underestimate PHN incidence compared to using the only study that reports this for Australians (MacIntyre 2015). The resubmission considered that any

assessment of the cost-effectiveness of RZV using a lower HZ incidence without adjusting the PHN risk will overestimate the ICER.

- 4.16 The October 2022 ATAGI pre-submission advice stated:
- 4.17 “The strength of the BEACH [MacIntyre] data is that it is representative of the target (national) population and captured using ICPC coding, which is considered a more robust approach. However, it may be subject to sampling bias with consecutive GP-patient encounters used to estimate HZ cases, resulting in an overestimation of population HZ incidence. The BEACH-only data has a marked increase for those over 80, which is not reflected in the PBS only, or BEACH & PBS adjusted data from the same paper. More recent Australian studies and the PBO arms of the ZOE trials do not show a similar sharp increase for those over 80 years of age”.
- 4.18 The difference in HZ incidence across the three potential sources of HZ incidence, particularly for individuals aged  $\geq 80$  years, is observed in Figure 1.

Figure 1: Summary of HZ incidence data by age group



Source: constructed from 7a. RZV ZONA CEA 65-69.70.80+ YOA.xls and 7b. RZV ZONA CEA 71-79, 71+ YOA.xls.

- 4.19 The base case ICER for individuals aged  $\geq 71$  years (\$5,000 to < \$15,000/QALY) incorporates the higher HZ incidence in individuals  $\geq 80$  years as reported in MacIntyre 2015. If it is assumed that the HZ and PHN incidence in individuals aged  $\geq 80$  years is the same as for individuals aged 71-79 years the ICER increases to \$15,000 to < \$25,000/QALY. The pre-PBAC response argued that it is stated in the Australian Immunisation Handbook, that ‘the risk and severity of outcomes increases with age’, including PHN, which ‘occurs in approximately 1 in 5 herpes zoster cases in people aged > 80 years, compared with approximately 1 in 10 cases in people aged 50-59 years’ (Australian Immunisation Handbook<sup>2</sup>). The pre-PBAC response also argued that

<sup>2</sup> Zoster (herpes zoster) | The Australian Immunisation Handbook (health.gov.au)

the majority of studies report an increasing trend in cumulative HZ incidence with age<sup>3,4</sup> and that age has been shown to be the strongest predictor of HZ incidence variation in a recently published meta-regression<sup>5</sup>. The pre-PBAC response suggested that estimates from MacIntyre 2015 or using a pooled incidence from MacIntyre 2015 & Qian 2021 may be appropriate to apply to the base case of the economic model. The pre-PBAC response stated that the risk of HZ plateaued in Qian 2021 for adults aged  $\geq 80$  years but increased in MacIntyre 2015, therefore the midpoint between these studies reduces the estimated increase in HZ incidence for individuals aged 70-79 years to  $\geq 80$  years. The pre-PBAC response argued that this estimate would be consistent with the broader body of evidence that reports on the relationship between age and HZ incidence but also results in a lowered HZ incidence estimate for all ages compared to MacIntyre 2015 alone.

- 4.20 The base case ICER for individuals aged  $\geq 80$  years (\$5,000 to < \$15,000/QALY) is lower than that for individuals aged 71 to 79 years (\$15,000 to < \$25,000/QALY). This reflects the higher HZ incidence in individuals  $\geq 80$  years as reported in MacIntyre 2015. The ICER for individuals aged  $\geq 80$  years when assuming the incidence of HZ and PHN is the same as in individuals aged 71 to 79 years is \$25,000 to < \$35,000/QALY. The cost effectiveness of RZV in individuals aged  $\geq 80$  years is dependent on the extent of additional risk of HZ and PHN in this population, compared to individuals aged 71 to 79 years.

**Scenario B: Individuals aged 65 to 69 years (and  $\geq 71$  years), cost per dose of \$**

- 4.21 The base case ICER for individuals aged 65 to 69 years with a cost per dose of \$ was \$5,000 to < \$15,000/QALY applying a 5% discount rate for costs and outcomes and \$5,000 to < \$15,000/QALY applying a 3.5% discount rate. Sensitivity analyses for the scenarios presented in the March 2023 PSD and noted in paragraph 4.7 above have been replicated in Table 6. The ICER for individuals aged  $\geq 71$  years with a cost per dose of \$ was \$5,000 to < \$15,000/QALY reduced from \$5,000 to < \$15,000/QALY with a cost per dose of \$.

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<sup>3</sup> van Oorschot D, Vroiling H, Bunge E, Diaz-Decaro J, Curran D, Yawn B. A systematic literature review of herpes zoster incidence worldwide. *Hum Vaccin Immunother.* 2021 Jun 3;17(6):1714-1732

<sup>4</sup> Kawai K, Gebremeskel BG, Acosta CJ. Systematic review of incidence and complications of herpes zoster: towards a global perspective. *BMJ Open.* 2014 Jun 10;4(6):e004833.

<sup>5</sup> Curran D, Callegaro A, Fahrback K, Neupane B, Vroiling H, van Oorschot D, Yawn BP. Meta-Regression of Herpes Zoster Incidence Worldwide. *Infect Dis Ther.* 2022 Feb;11(1):389-403

**Table 6: Results of sensitivity analyses for individuals aged 65 to 69 years (cost per dose of \$█)**

Analyses (per 1,000,000 individuals vaccinated)	Incremental cost (\$)	Incremental QALY	ICER (% change from base case)
<b>Base case</b>	█	8,615	█ <sup>1</sup>
Discount rate (base case 5% costs and outcomes)			
3.5% costs and outcomes	█	9,820	█ <sup>1</sup> (-29%)
HZ Incidence (base case MacIntyre 2015)			
MacIntyre 2015 + Qian 2021	█	7,780	█ <sup>2</sup> (+25%)
Qian 2021	█	6,939	█ <sup>2</sup> (+57%)
Vaccine efficacy (base case ZOE-50 and ZOE-70)			
Using effectiveness data from Izureita 2021	█	5,007	█ <sup>3</sup> (+167%)
RZV waning (base case ZOE-50, ZOE-70, ZOSTER-49)			
Alternate waning rate of 5.4% beginning at 10 years	█	7,310	█ <sup>2</sup> (+46%)
QALY loss for HZ & HZ with PHN (base case Gater 2014, Serpell 2014, Curran 2017)			
Lower 95% confidence interval	█	5,213	█ <sup>2</sup> (+65%)

Source: Table 3-3, Table 3-4, 7a. RZV ZONA CEA 65-69.70.80+ YOA.xls provided with resubmission. Constructed during the development of the submission overview.

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

The redacted values correspond to the following ranges:

<sup>1</sup> \$5,000 to < \$15,000

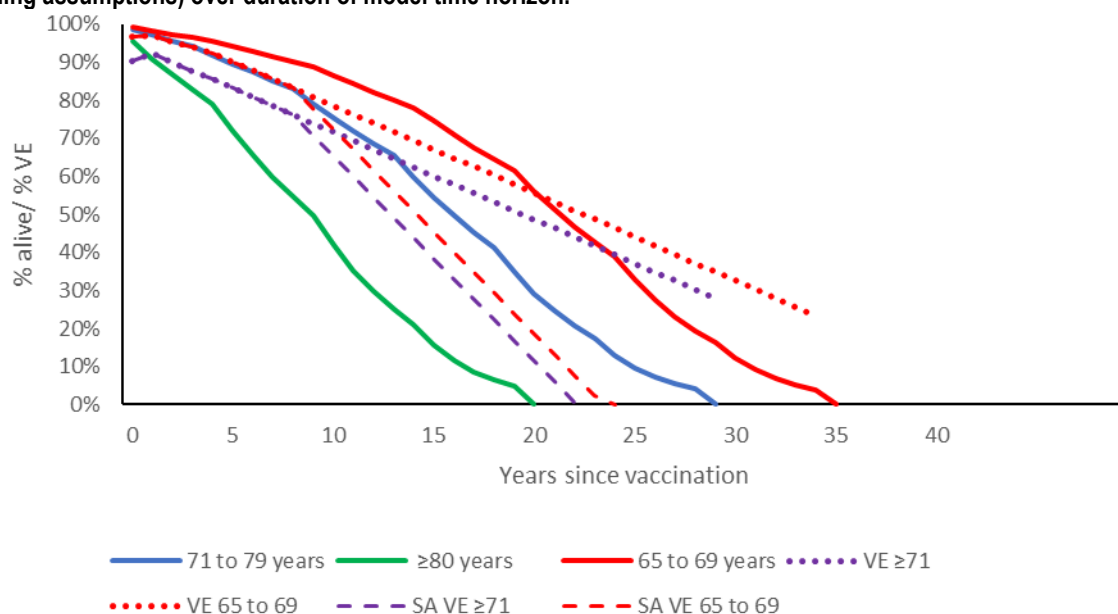
<sup>2</sup> \$15,000 to < \$25,000

<sup>3</sup> \$35,000 to < \$45,000

- 4.22 With a cost per dose of \$█ the ICERs for individuals aged 65-69 years ranged from \$15,000 to < \$25,000/QALY for the scenario with HZ incidence based on MacIntyre 2015 and Qian 2021 to \$35,000 to < \$45,000/QALY for the scenario with vaccine efficacy based on vaccine effectiveness in Izurieta 2021.
- 4.23 In March 2023 the PBAC noted the vaccine efficacy waning assumptions become more critical when vaccinating a younger cohort (paragraph 7.21, RZV PSD, March 2023 PBAC meeting). The ICER in individuals aged 65 to 69 years was more sensitive to changing assumptions regarding VE over time (i.e., waning) than in individuals aged 71 to 79 and ≥ 80 years (46% increase [Table 6] compared to 26% and 7% increase [Table 5], respectively).
- 4.24 Figure 2 overlays the proportion of individuals alive in each age cohort with VE over the duration of the modelled time horizon. Assumptions regarding waning only have a small impact on the ICER for individuals vaccinated at age ≥ 80 years because the vaccine is highly likely to remain effective for the remainder of the individuals' life. For example, VE remains above 50% for about 20 years, whereas median survival for the ≥ 80 year cohort is approximately 10 years. In contrast assumptions regarding waning have a larger impact on the ICER for individuals vaccinated at age 65-69 years as the rate of waning will impact on whether the vaccine remains effective for the remainder

of the individuals' life. For example, the median survival for the 65-69 year cohort is approximately 23 years, and with the resubmission's assumptions regarding waning, VE at 23 years is reduced to approximately 50%.

**Figure 2: Percent of individuals alive and vaccine efficacy (base case and sensitivity analysis using alternative waning assumptions) over duration of model time horizon.**



Source: generated from and 7a. RZV ZONA CEA 65-69.70.80+ YOA.xls and 7b. RZV ZONA CEA 71-79, 71+ YOA.xls provided with resubmission.  
SA = sensitivity analysis; VE = vaccine efficacy

4.25 The cost effectiveness of RZV in individuals aged 65 to 69 years is dependent on the long term VE of RZV. The waning assumptions in the economic model were based on up to 8 years of data from the first interim analysis of the ZOSTER-049 trial with assumed annual waning rates of 1.5% for adults before the age of 70 years and 2.3% for adults 70 years and older (with no change in waning rates dependent on time after vaccination) (paragraphs 6.45 to 6.51, RZV PSD, March 2023 PBAC meeting). If the annual waning rate 10 years after vaccination is increased to 5.4% per year the ICER increases to \$15,000 to < \$25,000/QALY. The pre-PBAC response stated that based on the ZOSTER-049 Y4 IA, overall RZV VE<sub>HZ</sub> was 89% (95% CI, 85.6%–91.3%), 1 month post-dose 2 in ZOE-50/70 to a mean of 9.6 (±0.3) years post-vaccination in the ZOE-50/-70 trials (Strezova, 2022)<sup>6</sup>.

<sup>6</sup> Strezova A, Diez-Domingo J, Al Shawafi K, Tinoco JC, Shi M, Pirrotta P, Mwakingwe-Omari A; Zoster-049 Study Group. 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. *Open Forum Infect Dis.* 2022 Oct 23;9(10):ofac485

### **Estimated NIP usage and financial implications**

- 4.26 As an early re-entry resubmission, the financial estimates were not independently evaluated.
- 4.27 The PBAC previously considered the estimated financial cost of listing RZV on the NIP for individuals aged 65 to 69 years and  $\geq 71$  years could reliably be determined using the estimates model provided in the resubmission (paragraph 7.25, RZV PSD, March 2023 PBAC meeting). The PBAC noted in any resubmission individuals previously vaccinated with 2 doses of RZV and individuals who have received ZVL in the previous 5 years should be removed from the estimates. This has been incorporated into the revised financial estimates (see Table 7). The PBAC previously noted the ATAGI post-submission advice indicated the proportion of the population that has previously received ZVL was higher than assumed in the resubmission. This was taken into account in the revised financial estimates (see Table 7).
- 4.28 The changes to the financial estimates are summarised in Table 7.

**Table 7: Changes to financial estimates**

<b>Parameter</b>	<b>March 2023 resubmission</b>	<b>July 2023 resubmission</b>
Cost per dose	\$█ for all age cohorts	\$█ for individuals aged 65 to 69 years \$█ for individuals aged $\geq 71$ years \$█ for individuals aged 70 years
Uptake of first dose	Cumulative first dose uptake in the non-Indigenous primary program for individuals aged 65 years was 75%.	Amended to a cumulative uptake of 65% (consistent with other age cohorts).
Individuals who have previously received 2 doses of RZV.	Not accounted for.	Assumed < 1% of age cohorts have received 2 prior doses of RZV.  Excluded from eligible population.
Individuals who have previously received 1 dose of RZV.	Not accounted for.	Assumed < 0.6% of age cohorts have received 1 prior dose of RZV.  Assumed this population would receive one dose of RZV funded by the NIP.
Individuals who have previously received ZVL	Assumed that 30% of individuals aged 70-79 years had received prior ZVL vaccination.  No limit on timing of prior ZVL before an individual could receive RVZ.	According to age cohort (see Table 8), with 50.5% of individuals aged 75 to 79 years assumed to have previously received ZVL.  Excludes individuals who have received ZVL in the last 5 years (see paragraph 4.33).
Immunocompromised population with conditions at high risk of HZ	Not accounted for.	89,025 individuals aged $\geq 65$ years excluded from eligible population.  Based on previous ATAGI post-submission advice that there is an estimated 126,170 immunocompromised individuals aged $\geq 18$ years with conditions at the high risk of HZ.

HZ = herpes zoster; NIP = National Immunisation Program; RVZ = recombinant zoster vaccine; ZVL = zoster vaccine live

- 4.29 The key inputs and sources for the financial estimates are presented in Table 8.

**Table 8: Key inputs for financial estimates**

Parameter	Value applied and source			
Eligible population	Eligible population based on ABS Population Projections, Australia, 2017 (base), (Series 3222.0)  Non-Indigenous population, reduced to account for immunocompromised individuals aged ≥ 18 years with conditions at high risk of HZ (recommended at March 2023 PBAC meeting) and individuals who have previously received 2 doses of RZV.			
Uptake rate: 1 <sup>st</sup> dose	Primary uptake: Yr 1: 47%, Yr 2: 55%; Yr 3 to Yr 6: 60%  Catch up uptake: variable uptake per year, dependent on whether an individual has had a prior HZ infection or received ZVL in the previous 5 years. Cumulative rate over 6 years is 65% in all populations			
Uptake rate: 2 <sup>nd</sup> dose	80.3%			
Assumptions	Prior ZVL	Prior RZV: 1 dose	Prior RZV: 2 doses	Prior HZ infection
Relevance	Individuals who have received in last 5 years excluded from eligible population (the numbers below are the overall % - see paragraph 4.33), based on AIR	Eligible for one dose of RZV on NIP, based on AIR (private sales data)	Individuals excluded from eligible population, based on AIR (private sales data)	Impacts uptake only
Aged 65 to 69 years	2.45%	0.54% (1.18%) <sup>a</sup>	0.87% (1.72%) <sup>a</sup>	24.2%
Aged 70 to 74 years	42.7%	0.60% (1.04%) <sup>b</sup>	0.99% (1.92%) <sup>b</sup>	32.9%
Aged 75 to 79 years	50.5%	0.33% (1.04%) <sup>b</sup>	0.57% (1.92%) <sup>b</sup>	
Aged ≥ 80 years	28.2%	0.26% (0.51%) <sup>c</sup>	0.43% (0.89%) <sup>c</sup>	49.7%
Cost of administration	Level A consultation MBS item 3 = \$18.20			

Source: Table 4-3, Table 4-8 in resubmission, Table 3 in pre-PBAC response

AIR = Australian Immunisation Register; HZ = herpes zoster; NIP = National Immunisation Program; RVZ = recombinant zoster vaccine; ZVL = zoster vaccine live

a Private market sales data reported for age group 60-69 years

b Private market sales data reported for age group 70-79 years

c Private market sales data reported for age group ≥ 80 years

4.30 The resubmission used information from the Australian Immunisation Registry (AIR) provided in the previous ATAGI post-submission advice to estimate the proportion of people in each age cohort who have ever received ZVL and at least one dose of RZV. In the resubmission, less than 2% of individuals in each age cohort were assumed to have been previously vaccinated with RZV. The pre-PBAC response provided updated financial estimates that included private RZV sales data available to the end of April 2023. These data suggest that the RZV uptake has been higher than reported in the AIR (Table 8). The pre-PBAC response noted that age was unknown for 20-25% of the private prescriptions and that the data did not capture hospital prescribing. Further, the analysis assumed all distributed RZV doses had been administered, however there may be excess stock in general practitioner or pharmacy fridges. Updated financial estimates are shown in the tables below.

4.31 Individuals who have received two or more doses of RZV were removed from the eligible population and those who had previously received 1 dose of RZV were assumed to only receive 1 additional NIP dose of RZV in Year 1, based on the 2nd dose completion rates (80.3%).

- 4.32 To determine the proportion of adults who have ever received ZVL would have received vaccination within 5 years, the resubmission made a simple assumption that ZVL uptake rates have been constant over time. As ZVL was NIP listed in November 2016, there will have been roughly 7 years of opportunity to receive ZVL since its NIP listing until the end of 2023. As such, the estimated age-specific proportion who have received ZVL after < 5 years in 2023 is  $5/7 \times$  age-specific % ever received ZVL, with the proportion decreasing for each following year ( $4/7$  in 2024,  $3/7$  in 2025, etc.).
- 4.33 Changes in healthcare resource utilisation which would accrue from NIP listing of RZV were excluded from the revised financial estimates in the resubmission.

**Scenario A: Individuals aged  $\geq 71$  years (catch-up program), cost per dose of \$** [REDACTED]

- 4.34 Table 9 summarises the overall estimated use and financial implications of including RZV on the NIP for individuals aged 70 years (recommended population at cost of \$ [REDACTED] per dose) and a catch up program in individuals aged  $\geq 71$  years. Based on the pre-PBAC response the estimated cost to the NIP is \$200 million to < \$300 million in the first year, \$90 million to < \$100 million in Year 6, totalling \$700 million to < \$800 million over 6 years. Table 9 also provides the NIP costs updated in the pre-PBAC response for vaccinating individuals aged 71-79 years (\$200 million to < \$300 million over 6 years) and  $\geq 80$  years (\$200 million to < \$300 million over 6 years). The pre-PBAC response stated that financial estimates include doses administered to adults aged 70 years at the PBAC recommended cost per dose of \$ [REDACTED]. However, it was also noted that uptake in individuals aged 70 years is assumed to be lower if there is an opportunity to receive RZV at an older age compared with RZV being available for adults aged 70 years without ongoing eligibility (the recommended population).

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Table 9: Estimated use and financial implications of listing RZV on the NIP for individuals aged 70 years (primary program) and ≥ 71 years (catch up program), cost per dose \$█

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
<b>Estimated extent of use</b>						
<b>Number of individuals vaccinated</b>						
Aged 70 years (pre-PBAC response)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)
Aged 71 to 79 years (pre-PBAC response)	2 (2)	1 (1)	1 (1)	3 (3)	4 (4)	5 (5)
Aged ≥ 80 years (pre-PBAC response)	6 (6)	1 (1)	1 (1)	7 (7)	8 (8)	1 (1)
Total (pre-PBAC response)	9 (9)	10 (10)	10 (10)	2 (2)	2 (2)	2 (2)
<b>Number of doses administered</b>						
Aged 70 years (pre-PBAC response)	1 (1)	6 (6)	6 (6)	6 (6)	6 (6)	6 (6)
Aged 71 to 79 years (pre-PBAC response)	9 (11)	2 (1)	2 (1)	1 (1)	1 (1)	1 (1)
Aged ≥ 80 years (pre-PBAC response)	12 (12)	6 (6)	6 (6)	1 (1)	1 (1)	1 (1)
Total (pre-PBAC response)	13 (13)	14 (9)	14 (14)	12 (12)	12 (12)	12 (12)
<b>Estimated financial implications of including RZV on the NIP</b>						
Aged 70 years (pre-PBAC response)	15 (15)	16 (16)	16 (16)	16 (16)	16 (16)	17 (16)
Aged 71 to 79 years (pre-PBAC response)	18 (18)	16 (16)	16 (16)	19 (19)	19 (19)	19 (19)
Aged ≥ 80 years (pre-PBAC response)	20 (20)	15 (15)	15 (15)	21 (21)	21 (21)	21 (21)
Total (pre-PBAC response)	22 (22)	18 (18)	18 (18)	23 (24)	23 (23)	23 (23)
<b>Estimated vaccine administration cost</b>						
Aged 70 years (pre-PBAC response)	25 (25)	25 (25)	25 (25)	25 (25)	25 (25)	25 (25)
Aged 71 to 79 years (pre-PBAC response)	19 (19)	25 (25)	25 (25)	25 (25)	25 (25)	25 (25)
Aged ≥ 80 years (pre-PBAC response)	25 (25)	25 (25)	25 (25)	25 (25)	25 (25)	25 (25)
Total (pre-PBAC response)	21 (21)	19 (19)	19 (19)	19 (19)	19 (19)	19 (19)

Source: Table 4-14 and calculated and financial estimates spreadsheet provided with pre-PBAC response, NIP = National Immunisation Program; RVZ = recombinant zoster vaccine

The redacted values correspond to the following ranges:

- 1 100,000 to < 200,000
- 2 300,000 to < 400,000
- 3 70,000 to < 80,000
- 4 60,000 to < 70,000
- 5 50,000 to < 60,000
- 6 200,000 to < 300,000
- 7 80,000 to < 90,000
- 8 90,000 to < 100,000
- 9 700,000 to < 800,000
- 10 400,000 to < 500,000
- 11 600,000 to < 700,000
- 12 500,000 to < 600,000
- 13 1,000,000 to < 2,000,000

<sup>14</sup> 800,000 to < 900,000

<sup>15</sup> \$30 million to < \$40 million

<sup>16</sup> \$40 million to < \$50 million

<sup>17</sup> \$50 million to < \$60 million

<sup>18</sup> \$100 million to < \$200 million

<sup>19</sup> \$10 million to < \$20 million

<sup>20</sup> \$70 million to < \$80 million

<sup>21</sup> \$20 million to < \$30 million

<sup>22</sup> \$200 million to < \$300 million

<sup>23</sup> \$90 million to < \$100 million

<sup>24</sup> \$80 million to < \$90 million

<sup>25</sup> \$0 to < \$10 million

**Scenario B: Individuals aged 65 to 69 years and  $\geq$  71 years, cost per dose of \$**

- 4.35 Table 10 summarises the overall estimated use and financial implications of including RZV on the NIP as a primary program for individuals aged 65 years and a catch up program in individuals aged  $\geq$  66 years. The estimated cost to the NIP based on the estimates included in the pre-PBAC response is \$200 million to < \$300 million in the first year, \$100 million to < \$200 million in Year 6, totalling \$900 million to < \$1 billion over 6 years. The pre-PBAC response stated that financial estimates shown in Table 10 include doses administered to adults aged 70 years at the PBAC recommended cost per dose of \$<sup>1</sup>. However, it is noted that uptake in individuals aged 70 years is assumed to be lower if there is an opportunity to receive RZV at an older age compared with RZV being available for adults aged 70 years without ongoing eligibility (the recommended population).

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Table 10: Estimated use and financial implications of listing RZV on the NIP for individuals aged 65 as a primary program with a catch up program for individuals aged ≥ 66, cost per dose \$█

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
<b>Estimated extent of use</b>						
<b>Number of individuals vaccinated</b>						
Aged 65 years (pre-PBAC response)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)
Aged 65 to 69 years (pre-PBAC response)	2 (2)	1 (1)	3 (3)	4 (4)	5 (5)	5 (5)
Aged 70 to 79 years (pre-PBAC response)	6 (6)	2 (2)	2 (2)	1 (1)	1 (1)	1 (1)
Aged ≥ 80 years (pre-PBAC response)	2 (2)	1 (1)	1 (1)	7 (7)	8 (8)	1 (1)
Total (pre-PBAC response)	9 (9)	10 (10)	10 (10)	11 (11)	12 (12)	12 (12)
<b>Number of doses dispensed</b>						
Aged 65 years (pre-PBAC response)	2 (2)	2 (2)	11 (11)	11 (11)	11 (11)	11 (11)
Aged 65 to 69 years (pre-PBAC response)	12 (12)	2 (2)	1 (1)	13 (14)	15 (15)	15 (15)
Aged 70 to 79 years (pre-PBAC response)	16 (16)	11 (11)	11 (11)	2 (1)	2 (2)	1 (1)
Aged ≥ 80 years (pre-PBAC response)	17 (17)	2 (2)	2 (2)	1 (1)	1 (1)	1 (1)
Total (pre-PBAC response)	18 (18)	9 (9)	9 (9)	19 (19)	19 (19)	19 (19)
<b>Estimated financial implications of including RZV on the NIP</b>						
Aged 65 years (pre-PBAC response)	20 (20)	20 (20)	21 (21)	21 (21)	21 (21)	21 (21)
Aged 65 to 69 years (pre-PBAC response)	22 (22)	20 (20)	23 (23)	24 (24)	24 (24)	24 (24)
Aged 70 to 79 years (pre-PBAC response)	30 (30)	25 (25)	25 (25)	23 (23)	20 (20)	23 (23)
Aged ≥ 80 years (pre-PBAC response)	26 (26)	20 (20)	20 (20)	23 (23)	23 (23)	23 (23)
Total (pre-PBAC response)	29 (29)	30 (30)	30 (30)	30 (30)	30 (30)	30 (30)
<b>Estimated vaccine administration cost</b>						
Aged 65 years (pre-PBAC response)	24 (24)	24 (24)	24 (24)	24 (24)	24 (24)	24 (24)
Aged 65 to 69 years (pre-PBAC response)	24 (24)	24 (24)	24 (24)	24 (24)	24 (24)	24 (24)
Aged 70 to 79 years (pre-PBAC response)	27 (27)	24 (24)	24 (24)	24 (24)	24 (24)	24 (24)
Aged ≥ 80 years (pre-PBAC response)	24 (24)	24 (24)	24 (24)	24 (24)	24 (24)	24 (24)
Total (pre-PBAC response)	20 (20)	28 (28)	28 (27)	27 (27)	27 (27)	27 (27)

Source: Table 4-15 in resubmission and financial estimates spreadsheet provided with pre-PBAC response

NIP = National Immunisation Program; RVZ = recombinant zoster vaccine

The redacted values correspond to the following ranges:

1 100,000 to < 200,000

2 200,000 to < 300,000

3 90,000 to < 100,000

4 20,000 to < 30,000

- <sup>5</sup> 10,000 to < 20,000
- <sup>6</sup> 400,000 to < 500,000
- <sup>7</sup> 80,000 to < 90,000
- <sup>8</sup> 90,000 to < 100,000
- <sup>9</sup> 1,000,000 to < 2,000,000
- <sup>10</sup> 600,000 to < 700,000
- <sup>11</sup> 300,000 to < 400,000
- <sup>12</sup> 400,000 to < 500,000
- <sup>13</sup> 50,000 to < 60,000
- <sup>14</sup> 40,000 to < 50,000
- <sup>15</sup> 20,000 to < 30,000
- <sup>16</sup> 800,000 to < 900,000
- <sup>17</sup> 500,000 to < 600,000
- <sup>18</sup> 2,000,000 to < 3,000,000
- <sup>19</sup> 700,000 to < 800,000
- <sup>20</sup> \$30 million to < \$40 million
- <sup>21</sup> \$40 million to < \$50 million
- <sup>22</sup> \$60 million to < \$70 million
- <sup>23</sup> \$20 million to < \$30 million
- <sup>24</sup> \$0 to < \$10 million
- <sup>25</sup> \$50 million to < \$60 million
- <sup>26</sup> \$70 million to < \$80 million
- <sup>27</sup> \$10 million to < \$20 million
- <sup>28</sup> \$20 million to < \$30 million
- <sup>29</sup> \$200 million to < \$300 million
- <sup>30</sup> \$100 million to < \$200 million

For more detail on PBAC’s view, see section 5 PBAC outcome.

## 5 PBAC Outcome

- 5.1 The PBAC recommended that varicella zoster virus recombinant vaccine (RZV, Shingrix®) be a designated vaccine for the purposes of the *National Health Act 1953*, for the prevention of herpes zoster (HZ) and post-herpetic neuralgia (PHN) for individuals aged 65 years (primary program) and older (catch-up program). RZV will be listed on the National Immunisation Program (NIP) as of the 1 November 2023 for individuals aged 70 years (based on the PBAC’s March 2023 recommendation). The PBAC considered, based on the reduced price proposed, that RZV is cost-effective with the age for the primary program lowered to 65 years and with there being no upper age limit for the catch-up program. The PBAC noted the cost effectiveness relies on accepting the long term modelled vaccine efficacy (VE), and in this context considered that the cost-effectiveness of RZV should be reassessed if a booster dose is required or if long-term efficacy is less than predicted. The PBAC noted the total cost of the program was high.
- 5.2 The PBAC noted the consumer comments were supportive of expanding the currently approved access to RZV on the NIP. The PBAC noted the comments highlighting the importance of having a safe and effective vaccine available to a broader population. The PBAC noted a number of comments raised the equity issues currently associated with the high cost of RZV on the private market.

- 5.3 The PBAC noted the live zoster vaccine (ZVL, Zostavax) is currently listed on the NIP for individuals aged 70 years with a catch up program in place for individuals aged at least 71 years and less than 80 years of age until 31 October 2023. The PBAC noted that from 1 November 2023 RZV will be available on the NIP for non-Indigenous individuals aged 70 years, Aboriginal and Torres Strait Islander individuals aged  $\geq 50$  years and immunocompromised individuals aged  $\geq 18$  years with conditions at high risk of HZ infection. Conditions with a high risk of HZ infection included haemopoietic stem cell transplant, solid organ transplant, haematological malignancy and advanced or untreated HIV.
- 5.4 The PBAC reaffirmed its March 2023 advice that the clinical claim that RZV is superior in terms of effectiveness and slightly inferior in terms of safety compared to placebo for the proposed NIP populations was reasonable.
- 5.5 The PBAC recalled at the March 2023 meeting that it did not recommend RZV for non-Indigenous individuals aged 65 to 69 years and  $\geq 71$  years as it had considered in the context of the total cost that the extent of uncertainty regarding the cost-effectiveness of RZV to be too high and that a price reduction would be required for the RZV to be considered cost-effective for these populations (paragraphs 7.21, March 2023 RVZ PBAC PSD). The PBAC noted the resubmission considered the cost-effectiveness of the two requested age cohorts separately (individuals aged 65 to 69 years and  $\geq 71$  years). The PBAC noted a reduced price of \$| per dose was proposed for RZV, compared with \$| in the March 2023 submission, although the price proposed for the  $\geq 71$  year cohort was higher (\$| per dose) in the event that listing for individuals aged 65 to 69 years was either not recommended or recommended but implemented later than the listing for individuals aged  $\geq 71$  years (assumed one year later in the resubmission). The PBAC noted that the timing of inclusion on the NIP is not a matter for its consideration. However, as outlined in paragraph 5.7 below, the PBAC noted the ICERs were similar for the cohorts aged 65-69 years and  $\geq 71$  years and therefore did not consider that a higher price was justified for RZV in the older cohort.
- 5.6 **Individuals aged  $\geq 71$  years:** The PBAC noted that the base case ICER was \$5,000 to  $< \$15,000$  per quality adjusted life year (QALY) with a cost per dose of \$| and \$5,000 to  $< \$15,000$ /QALY with a cost per dose of \$|. The PBAC noted the ICER was sensitive to the extent of the increase in HZ incidence in individuals aged  $\geq 80$  years (Table 5) and that the increase may have been overestimated with the use of MacIntyre 2015 alone to inform incidence. The pre-PBAC response acknowledged this remained an area of uncertainty and suggested consideration of the pooled data from MacIntyre 2015 and Qian 2021 as this resulted in a relationship of age and HZ risk that was consistent with the broader body of evidence (and results in a lower HZ incidence for all age groups, Figure 1). The ICER using the pooled HZ incidence data was \$15,000 to  $< \$25,000$ /QALY with a cost per dose of \$| and \$15,000 to  $< \$25,000$ /QALY with a cost per dose of \$|. The PBAC considered RZV to be acceptably cost-effective in individuals aged  $\geq 71$  years based on the range of ICERs presented in Table 4 and Table 5. The PBAC noted the ICERs were similar for the cohorts aged 71-79 years and  $\geq 80$  years (\$15,000 to

< \$25,000/QALY and \$15,000 to < \$25,000/QALY respectively with a cost per dose of \$| and \$15,000 to < \$25,000/QALY and \$15,000 to < \$25,000/QALY respectively with a cost per dose of \$|) and hence considered there was no basis to exclude the older age group from the NIP listing.

- 5.7 **Individuals aged 65-69 years:** The PBAC noted that the base case ICER was \$5,000 to < \$15,000/QALY with a cost per dose of \$|, and that this increased to \$15,000 to < \$25,000/QALY with HZ incidence informed by both MacIntyre 2015 and Qian 2021. The PBAC noted this was similar to the ICER for the ≥ 71 year cohort (\$15,000 to < \$25,000/QALY at \$| per dose) and on this basis considered RZV to be cost-effective in the 65-69 year cohort. However, the PBAC noted the cost effectiveness of RZV in individuals aged 65 to 69 years is dependent on accepting the long term VE as assumed in the economic model (Figure 2), and reiterated its advice from the March 2023 meeting that the long-term efficacy of RZV should be monitored and the cost-effectiveness reconsidered if a booster dose is required or if long-term efficacy is less than predicted.
- 5.8 The PBAC considered the estimated financial cost of listing RZV on the NIP for non-Indigenous individuals aged 65 to 69 years and ≥ 71 years could reliably be determined using the estimates model provided in the resubmission. The PBAC noted in line with its previous advice that the resubmission had removed individuals previously vaccinated with 2 doses of RZV and individuals who had received ZVL in the previous 5 years from the financial estimates, and amended the proportion of individuals who had previously received ZVL based on the March 2023 ATAGI post-submission advice. The PBAC noted that the pre-PBAC response provided estimates of prior use of RZV based on sales data and considered this a more reliable source given that the Australian Immunisation Registry (AIR) appears to underestimate private uptake of vaccines. The PBAC noted with a cost per dose of \$| and implementing the NIP listing for all individuals aged 65 years and above simultaneously, that the estimated cost to the NIP is \$200 million to < \$300 million in the first year, \$100 million to < \$200 million in Year 6, totalling \$900 million to < \$1 billion over 6 years. The PBAC noted these estimates include the cost of vaccinating individuals aged 70 years (at a cost of \$| per dose) as recommended in March 2023.
- 5.9 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:**

Recommended

## 6 Recommended listing

- 6.1 Add new item to the Determination:

Vaccine and the circumstances in which vaccine may be provided	Brand	Formulation	Number and timing of doses
recombinant varicella zoster virus glycoprotein E antigen (AS01B Adjuvanted) vaccine	Shingrix	powder and suspension for injection, 0.5 mL	<ul style="list-style-type: none"> <li>a. Two primary doses 2 to 6 months apart</li> <li>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</li> <li>c. Those eligible populations who have received one dose privately can receive their second dose on the NIP</li> </ul>

**Circumstances**

Vaccine may be provided to a person who:

- (a) is at least 65 years of age AND
- (b) has not been vaccinated with Zostavax in the past 5 years or with 2 doses of Shingrix

***The wording of the item may be subject to further review. Should there be any changes made to the item the sponsor will be informed.***

## 7 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.

## 8 Sponsor’s Comment

GSK welcomes both the PBAC recommendation of Shingrix for older adults and their recognition of the value of preventive options against shingles and its associated complications. We look forward to working with the PBAC to expand NIP eligibility for other cohorts of Australian adults at increased risk of shingles.