

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

1 Background

- 1.1 At its March 2023 meeting, the PBAC recommended that varicella zoster virus recombinant vaccine (RZV) be a designated vaccine for the purposes of the *National Health Act 1953* 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 (as defined by ATAGI in its post-submission advice). The PBAC deferred a decision for a broader population of immunocompromised individuals aged ≥ 18 years at increased risk of HZ infection to seek further ATAGI advice on the appropriate definition of this population. The PBAC did not recommend RZV for non-Indigenous individuals aged 65 to 69 years and aged ≥ 71 years.
- 1.2 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 years of age (primary program) and older (catch-up program).
- 1.3 On 1 November 2023¹, RZV was included on the NIP for:
 - People aged 65 years and older;
 - Aboriginal and Torres Strait Islander people aged 50 years and older;
 - Immunocompromised people aged 18 years and older with the following medical conditions (i) haemopoietic stem cell transplant (ii) solid organ transplant (iii) haematological malignancy and (iv) advanced or untreated HIV.
- 1.4 In response to the PBAC's March 2023 deferral for the broader population of immunocompromised individuals at increased risk of HZ infection, ATAGI provided advice in September 2023 which outlined a number of additional conditions and immunosuppressive therapies which it considered conferred a moderate or high risk for HZ, both categories which ATAGI considered appropriate for funded vaccination with RZV.
- 1.5 The nationally negotiated price (NNP) (as recommended by the PBAC) for people aged 65 years and older is \$| per dose. For people aged 70 years, Aboriginal and Torres Strait

¹ <https://www.health.gov.au/news/national-immunisation-program-changes-to-shingles-vaccination-from-1-november-2023>

Islander people aged 50 years and older and immunocompromised people aged 18 years and older (as outlined in paragraph 1.3) the NNP is \$.

2 Requested listing

2.1 The sponsor proposed the following criteria for RZV.

Vaccine and the circumstances in which vaccine may be provided	Brand	Formulation	Number and timing of doses
Recombinant varicella zoster virus glycoprotein E antigen (AS01 _B Adjuvanted) vaccine	Shingrix	Powder and suspension for injection, 0.5 mL	<p>a) unless paragraph (b) applies, 2 primary doses with the second dose given 2 to 6 months after the first dose</p> <p>b) For persons who are immunodeficient, immunosuppressed or likely to become immunosuppressed due to known disease or therapy, 2 primary doses can be given 1 to 2 months apart</p> <p>c) Those eligible populations who have received one dose privately can receive their second dose on the NIP</p>

Circumstances

Vaccine may be provided to a person who:

- (a) is at least 65 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,
 - i. due to an underlying condition and/or immunomodulatory/immunosuppressive treatments as specified in subsection 7; or
 - ii. due to treatment with systemic corticosteroids (≥ 10 mg/day prednisolone equivalent dose) and considered by the treating physician to be at comparable risk to an individual in paragraph i.; or
 - iii. as determined by the treating physician to be at comparable risk to an individual in paragraph i.

For more detail on PBAC's view, see section 4 PBAC outcome.

3 Consideration of the evidence

Sponsor hearing

3.1 There was no hearing for this item.

Consumer comments

3.2 The PBAC noted and welcomed the input from health care professionals (1) and organisations (6) via the Consumer Comments facility on the PBS website. The health care professional noted that RZV is a more effective vaccine than the live varicella zoster vaccine and can be used in immunocompromised individuals which is a significant advantage. The health care professional considered the current cost of RZV on the private market to be a disadvantage.

3.3 The PBAC noted and welcomed the input from the Australian Rheumatology Association (ARA), Multiple Sclerosis (MS) Australia, Crohn's and Colitis Australia (CCA), Lung Foundation Australia, Immunisation Coalition Scientific Advisory Committee and Kidney Health Australia.

- 3.4 The ARA noted that while all immunocompromised patients are at higher risk, the reactivation of varicella zoster virus is the most concerning infective complication in people treated with Janus kinase inhibitors, which places rheumatology patients taking this class of medicines at even greater risk. The ARA noted there are disease-associated risks e.g., SLE, inflammatory myositis and RA, that are independent of age and medication-related risk. The ARA stated it understands including diseases with a spectrum of activity is challenging, but would like to highlight for consideration in future iterations the risk of the patients who would be excluded solely based on age in the current proposal.
- 3.5 MS Australia noted some people with MS are considered to be severely immunocompromised because of medications they may be receiving to treat their MS. MS Australia noted RZV offers an effective, inactivated vaccine suitable for the wider immunocompromised population over the age of 18, including individuals with MS on specific disease modifying therapies. The organisation strongly supported its inclusion on the NIP for the broader immunocompromised population over the age of 18 years.
- 3.6 CCA supported the inclusion of RZV on the NIP for vaccination of people living with Crohn's disease and ulcerative colitis. CCA noted that people with inflammatory bowel disease (IBD) are at higher risk of HZ infection than those who do not and people with IBD taking immunosuppressants are at even higher risk of HZ infection.
- 3.7 Lung Foundation Australia supported people with chronic obstructive pulmonary disease (COPD) being included in the population of immunocompromised individuals who can access RVZ on the NIP. The Foundation stated that preventing infection in people living with COPD is vital to reduce exacerbation of symptoms that can lead to hospitalisation and poorer prognosis.
- 3.8 Kidney Health Australia noted the importance of vaccination against HZ for people on dialysis and prior to transplantation.
- 3.9 The Immunisation Coalition Scientific Advisory Committee wrote in support stating the vaccine was safer than live vaccines, could be given to those who are immunosuppressed and was more effective over a longer duration.
- 3.10 The PBAC noted there were many comments regarding the high cost of RVZ when privately funded.

ATAGI advice: September 2023

- 3.11 The ATAGI defined additional conditions and immunosuppressive therapies with a high risk for HZ, and classified those which confer a moderate risk, both categories which ATAGI considered appropriate for funded vaccination with RZV.
- 3.12 The ATAGI sought the advice of the Australian Society of Clinical Immunology and Allergy and received submissions from key patient advocacy groups including the ARA. Expert opinion was supplemented with a review of available literature on immunocompromising conditions and immunosuppressive therapies, and risk of HZ.

3.13 The ATAGI advice stated the following considerations had been taken into account in evaluating the risks of HZ and identifying the appropriate population to consider for funding:

- Age is one of the greatest determinants of individual risk, confounding the risk due to other causes.
- An individual's risk may be determined by a multiplicity of differing factors including multiple therapies, comorbidities, their history of previous varicella infection or HZ, and age.
- There is no standardised classification of levels of immunocompromise.
- The degree of immunocompromise may be related both to a patient's underlying condition(s) (primary or acquired) or from their immunosuppressive therapies.
- The level of immunocompromise may change during various time periods of treatment, e.g. at treatment induction, during cycles of treatment, or during maintenance therapy.
- The duration of immunocompromise, noting that some individuals may be immunocompromised only during a certain period of treatment while others with chronic conditions may remain immunocompromised over a long period.
- The use of mitigation strategies such as antiviral prophylaxis with certain conditions.
- The expanding number of new immunosuppressive therapies, particularly biologic therapies, and their increasing usage, often with limited published evidence of their risk of HZ.

3.14 For each condition or therapy in Table 1, the ATAGI considered the risk of herpes zoster to be sufficiently elevated compared to a person without that condition or therapy, or to the general population, as to warrant vaccination.

Table 1: Conditions and therapies associated with an increased risk of herpes zoster and their estimated population sizes as defined by ATAGI.

Condition or therapy	Population size
Additional high risk conditions	
Inborn errors of immunity with ongoing functional deficits including: <ul style="list-style-type: none"> • Humoral e.g. X-linked agammaglobulinemia • Combined defects e.g. Severe Combined Immunodeficiency (SCID) • Phagocytic disorders e.g. Chronic Granulomatous Disease (CGD) • Other inborn errors of immunity except complement disorders, hereditary angioedema (HAE) and IgA deficiency (considered lower risk). 	16,700
End stage renal disease/renal failure/chronic kidney disease on dialysis	28,542
Additional high risk therapies	
B and T-cell targeted monoclonal antibody therapies, currently or within the last 6 months, including: <ul style="list-style-type: none"> • anti-CD20 • anti B-cell activating factor (BAFF) • anti-CD52 • Anti-thymocyte globulin 	19,750
Conventional immunosuppressive agents currently or within the last 6 months, such as: <ul style="list-style-type: none"> • high dose methotrexate ≥ 20mg per week (oral and subcutaneous) • azathioprine ≥ 3.0mg/kg/day • 6-mercaptopurine ≥ 1.5mg/kg/day • mycophenolate ≥ 1g/day • cyclophosphamide • systemic calcineurin inhibitors (tacrolimus, cyclosporin) • mTOR inhibitors • Purine analogues (cladribine) 	71,085
Biologic therapies (except those listed as moderate or lower risk), currently or within the last 6 months, such as tumour necrosis factor inhibitors (TNFi), T-cell co-stimulation modulators (e.g. Abatacept), soluble TNF receptors, Type I Interferon receptor inhibitors, proteasome inhibitors	72,231
Immunomodulatory drugs including Sphingosine-1-phosphate receptor modulators within the last 6 months	4,913
Oral small molecule targeted therapies, currently or within the last 6 months including Bruton's tyrosine kinase (BTK) inhibitors, Janus kinase (JAK) inhibitors, BCR-ABL inhibitors	31,496
Total additional high risk individuals	244,717
Moderate risk therapies	
Immunosuppressive therapy for solid organ tumours, currently or within the last 6 months: <ul style="list-style-type: none"> • conventional chemotherapy 	60,338
Interleukin (IL) inhibitors (except those listed as moderate or lower risk), currently or within the last 6 months, including Anti-IL1 antibodies, Anti-IL4/13 antibodies, Anti-IL5 antibodies, Anti-IL6 antibodies, IL-6 receptor inhibitors	23,063
Total moderate risk individuals	83,401

Source: Table 1, September 2023 ATAGI advice

3.15 The ATAGI noted that all population estimates presented in Table 1 include the populations previously recommended by the PBAC (as outlined in paragraphs 1.1 and 1.2). Other limitations include:

- potential over-estimation due to individuals being included in counts for their condition and their therapy and individuals receiving multiple eligible therapies;

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- potential underestimation due to patients receiving immunosuppressive therapies not funded under the PBS;
 - certain medications have immunosuppressive effects related to the dose received, and estimated numbers are likely overestimated due to inclusion of individuals receiving low doses which may not be sufficiently immunosuppressive i.e., it is not possible to obtain accurate unique population numbers for some conventional immunosuppressants with dose threshold-related inclusion in the high/moderate risk groups.
- 3.16 The ATAGI acknowledged that there may be additional conditions or categories that contain immunocompromised individuals, but these are expected to involve small numbers of individuals.
- 3.17 The ATAGI advised that where new medications become available within a class of therapy included in the determination, they will be automatically included in the list of eligible therapies for funded RZV. The PBAC noted additional advice (from ATAGI and PBAC) will be required to include a new medication class in the determination.
- 3.18 The ATAGI amended the description used to identify the cohort of people living with HIV that it considered should be eligible for RZV on the NIP, including changing the CD+ cell count from $< 250 / \mu\text{L}$ to $< 200 / \mu\text{L}$ (discussed further in paragraph 3.31). The ATAGI also included individuals who have received chimeric antigen receptor T-cell therapy in the list of cellular therapies.
- 3.19 The ATAGI also defined a group with lower risk for HZ who are still recommended for, and would benefit from RZV, but for whom funded vaccination is considered of lesser priority at present (Table 2).

Table 2: Conditions and therapies associated with a lower risk of herpes zoster and their estimated population sizes as defined by ATAGI.

Condition or therapy	Population size
Lower risk conditions	
Lower risk inborn errors of immunity <ul style="list-style-type: none"> • Complement disorders including HAE • IgA deficiency 	48,090
Lower risk therapies	
Lower risk biologic therapies currently or within the last 6 months: <ul style="list-style-type: none"> • Anti-integrins e.g. natalizumab and vedolizumab, • Anti-IgE antibodies • Anti-complement antibodies 	287,312
Lower risk interleukin inhibitors [†] , currently or within the last 6 months: <ul style="list-style-type: none"> • anti-IL17 antibodies, • anti-IL 12/23 antibodies, • anti-IL23 antibodies, and • anti-IL31 antibodies. 	
Conventional immunosuppressants/immunomodulatory drugs currently or within the last 6 months including: <ul style="list-style-type: none"> • Hydroxychloroquine • Leflunomide • Penicillamine • Auranofin • Aminosalicylates e.g. sulfasalazine 	
Solid organ tumours currently or within the last 6 months, receiving other active therapy including: <ul style="list-style-type: none"> • Kinase inhibitors (e.g. ALK inhibitors, CDK inhibitors) • Immune checkpoint inhibitors 	
• radiotherapy (alone, without concurrent or sequential chemotherapy)	73,797
Total lower risk population	409,200

ALK = anaplastic lymphoma kinase; CDK = cyclin dependent kinase; HAE = hereditary angioedema; IgE = immunoglobulin E; IL = interleukin
Source: Table 1, September 2023 ATAGI advice

Information provided by the sponsor

- 3.20 The sponsor provided input on the expanded list of cohorts identified by ATAGI and information to support the cost-effectiveness and associated financial implications for the NIP as requested by the PBAC in March 2023. Further ATAGI advice was sought following receipt of information from the sponsor.
- 3.21 The sponsor proposed a cost per dose of \$ [REDACTED] for the high risk population and \$ [REDACTED] for the moderate risk population. The sponsor stated that given the paucity of evidence to inform a cost-effectiveness model in the numerous sub-populations of adults at increased risk of HZ identified by ATAGI, previous recommendations from the March 2023 PBAC meeting and July 2023 PBAC meeting were used as a frame of reference for cost-effectiveness within the proposed additional cohorts.
- 3.22 The sponsor’s estimated total number of moderate and high risk individuals eligible for vaccination was largely consistent with the ATAGI estimates with the exception of the inclusion of 40,000 to < 50,000 high risk individuals estimated to be on high dose methotrexate.

- 3.23 The assumed growth in the number of eligible individuals in the high risk cohort was 3.7% to 3.8% per year and in the moderate risk cohort was 4.4% per year (compared to no growth assumed for the high risk cohort recommended in March 2023). Other assumptions were consistent with the high risk cohort recommended in March 2023.
- 3.24 The PBAC noted the estimates in Table 2 include non-Indigenous people aged 65 years and older and Aboriginal and Torres Strait Islander people aged 50 years and older who are able to access RZV on the NIP from 1 November 2023.
- 3.25 For the high and moderate risk cohorts (as defined by ATAGI, plus the additional high dose methotrexate population), over six years, there were an estimated 300,000 to < 400,000² persons vaccinated and 500,000 to < 600,000 doses administered. Applying the effective prices to each risk group resulted in a cost to NIP of \$90 million to < \$100 million. These cohorts replaced 100,000 to < 200,000³ persons within the existing recommended NIP populations who are projected to receive RZV, resulting in a total offset of 100,000 to < 200,000 doses and cost to NIP of \$20 million to < \$30 million. The final incremental impact of the ATAGI base case was an additional 200,000 to < 300,000 persons vaccinated, 300,000 to < 400,000 doses administered, and a cost to the NIP of \$60 million to < \$70 million.
- 3.26 The PBAC noted the financial estimates presented in Table 1 include high and moderate risk non-Indigenous individuals over 65 years of age and Aboriginal and Torres Strait Islander individuals over 50 years of age who currently have access to RZV on the NIP. A summary of the number of vaccinated individuals in the current and new cohort is provided in

² Calculated as 100,000 to < 200,000 + 60,000 to < 70,000

³ Calculated as 90,000 to < 100,000 + 500 to < 5,000

- 3.27 Table 3. Additionally, the PBAC noted individuals over 65 years of age that met the high risk criteria were included in the financial estimates for the additional cohort at \$1 per dose, and offset in the existing cohort at \$1 per dose. Therefore, the PBAC considered the stated incremental cost of \$60 million to < \$70 million was substantially overestimated.

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Table 3: Summary of number of vaccinated individuals, current and new cohort

Number of vaccinated individuals on the NIP	Current cohort	Including new cohort	Difference
Additional cohorts			
- High risk individuals ≥ 18 years of age	-	1	+ 1
- Moderate risk individuals ≥ 18 years of age	-	2	+ 2
Existing cohorts			
- Non-Indigenous individuals ≥ 65 years of age	3	3	- 6
- Aboriginal and Torres Strait Island individuals ≥ 50 years of age	4	4	- 7
- High risk individuals ≥ 18 years of age	4	4	-
Total	3	5	+ 1

Source: Calculated using Budget impact model - 'Results summary' worksheet,
The redacted values correspond to the following ranges:

¹ 200,000 to < 300,000

² 60,000 to < 70,000

³ 3,000,000 to < 4,000,000

⁴ 100,000 to < 200,000

⁵ 4,000,000 to < 5,000,000

⁶ 90,000 to < 100,000

⁷ 500 to < 5,000

Table 4: Financial estimates results: ATAGI base-case (high-risk IC and moderate-risk IC)

Population	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Total
Persons vaccinated							
Additional NIP cohorts	1	2	3	3	4	4	5
High-risk IC ≥18 YOA	6	7	8	8	9	9	10
Moderate-risk IC ≥18 YOA	4	9	11	11	11	11	12
Existing NIP cohorts	13	14	14	15	15	15	16
Non-Indigenous ≥65 YOA	13	14	17	5	5	5	16
First Nations People ≥50 YOA	3	4	4	9	9	9	1
High-risk IC ≥18 YOA (Mar-23 recommendation)	3	4	9	9	11	11	1
Total	13	18	14	15	15	15	19
Doses administered							
Additional NIP cohorts	10	1	2	2	8	3	17
High-risk IC ≥18 YOA	1	1	7	7	8	8	15
Moderate-risk IC ≥18 YOA	8	4	9	9	11	11	1
Existing NIP cohorts	16	13	13	18	18	18	20
Non-Indigenous ≥65 YOA	13	13	13	14	18	18	20
First Nations People ≥50 YOA	2	3	8	4	4	4	10
High-risk IC ≥18 YOA (Mar-23 recommendation)	2	3	4	4	9	9	1
Total	16	13	13	21	18	18	22
Cost to NIP							
Additional NIP cohorts	23	24	25	25	26	26	27
High-risk IC ≥18 YOA	24	25	25	25	26	26	28
Moderate-risk IC ≥18 YOA	26	26	26	26	26	26	25
Existing NIP cohorts	29	31	31	31	31	31	32
Non-Indigenous ≥65 YOA	30	31	31	27	31	31	32
First Nations People ≥50 YOA	25	26	26	26	26	26	33
High-risk IC ≥18 YOA (Mar-23 recommendation)	25	26	26	26	26	26	23
Total	29	30	31	31	31	31	34

IC = immunocompromised, NIP = National Immunisation Program, YOA = years of age.

Source: Budget impact model - 'Results summary' worksheet, rows 4:31 (must select High-Risk and Moderate-Risk IC and exclude systemic corticosteroids in the 'Inputs' worksheet)

The redacted values correspond to the following ranges:

¹ 100,000 to < 200,000

² 70,000 to < 80,000

³ 40,000 to < 50,000

⁴ 20,000 to < 30,000

⁵ 300,000 to < 400,000

⁶ 90,000 to < 100,000

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- ⁷ 50,000 to < 60,000
- ⁸ 30,000 to < 40,000
- ⁹ 10,000 to < 20,000
- ¹⁰ 200,000 to < 300,000
- ¹¹ 5,000 to < 10,000
- ¹² 60,000 to < 70,000
- ¹³ 1,000,000 to < 2,000,000
- ¹⁴ 600,000 to < 700,000
- ¹⁵ 400,000 to < 500,000
- ¹⁶ 2,000,000 to < 3,000,000
- ¹⁷ 500,000 to < 600,000
- ¹⁸ 700,000 to < 800,000
- ¹⁹ 4,000,000 to < 5,000,000
- ²⁰ 6,000,000 to < 7,000,000
- ²¹ 800,000 to < 900,000
- ²² 7,000,000 to < 8,000,000
- ²³ \$30 million to < \$40 million
- ²⁴ \$20 million to < \$30 million
- ²⁵ \$10 million to < \$20 million
- ²⁶ \$0 to < \$10 million
- ²⁷ \$90 million to < \$100 million
- ²⁸ \$70 million to < \$80 million
- ²⁹ \$300 million to < \$400 million
- ³⁰ \$200 million to < \$300 million
- ³¹ \$100 million to < \$200 million
- ³² \$900 million to < \$1 billion
- ³³ \$40 million to < \$50 million
- ³⁴ > \$ 1 billion

Additional high risk populations proposed by the sponsor

- 3.28 The sponsor proposed inclusion of the following individuals in the funded populations, in addition to the populations recommended by ATAGI. Further ATAGI advice was provided addressing the issues raised by the sponsor.
- 3.29 Those on a daily dose of ≥ 10 mg of prednisolone (or equivalent) (criteria and financial estimates were provided for this population). The submission noted the ATAGI had previously advised that individuals receiving regular higher doses of systemic corticosteroids are at a high risk of HZ (paragraph 4.3, RZV Public Summary Document (PSD), March 2023 PBAC meeting). The ATAGI did not support inclusion of individuals receiving ≥ 10 mg prednisolone (or equivalent) for NIP funding. The ATAGI noted the risk arising from this use alone is likely to be short-term. In most clinical situations people requiring longer term use of moderate to high-dose systemic corticosteroids, and therefore at sustained increased risk of HZ, are likely to be transitioned to an alternate ‘steroid sparing’ therapy, which would likely be eligible for inclusion in the new high or moderate risk categories.
- 3.30 Those aged 50 to 64 years of age with inflammatory bowel disease (IBD) or diabetes. Large observational studies cited in previous ATAGI advice suggested that individuals with IBD and diabetes aged 50-64 years of age have a similar or higher level of risk as the general population ≥ 65 years of age. The ATAGI did not support inclusion of individuals with IBD or diabetes for NIP funding, based on the diagnosis alone. ATAGI noted that those with IBD are at increased risk of HZ but advised it was appropriate that some risk populations (including IBD) be defined by therapy and not just by the risk condition itself. ATAGI did not find evidence of high or moderate certainty to support an increased risk of HZ in people with diabetes that was not heavily confounded by age.
- 3.31 Those with chronic kidney disease with renal failure who are not receiving dialysis. The sponsor noted the ATAGI advice reported a risk ratio of 2.14 for chronic kidney disease (CKD) patients with renal failure (Hata, 2011), and a risk ratio of 1.98 for CKD patients on dialysis (no reference provided) (Sep-23 ATAGI advice, Appendix Table 1). However, only CKD patients on dialysis were included in ATAGI’s definition of high-risk patient groups, despite reporting a higher risk ratio for CKD with renal failure. The ATAGI acknowledged the sponsor’s comments regarding patients with chronic kidney disease. Noting the two key studies from which the risk estimates were derived were in patients on long-term dialysis⁴ and patients with renal failure⁵ the ATAGI supported revising the recommended description/definition of the cohort, to “End stage renal disease (Stage 5 chronic kidney disease) or on long-term dialysis”.

⁴ Kuo CC, Lee CT, Lee IM et al. Risk of herpes zoster in patients treatment with long-term hemodialysis: a matched cohort study. *American Journal of Kidney Diseases* 2012; 59: 428 – 33.

⁵ Hata A, Kuniyoshi M, Ohkusa Y. Risk of herpes zoster in patients with underlying diseases: a retrospective hospital-based cohort study. *Infection* 2011; 39: 537-44

- 3.32 Those living with HIV, regardless of CD4 counts. The sponsor noted the ATAGI advice amended the population of individuals with HIV infection, with a threshold CD4 cell count lowered to <200/ μ L from <250/ μ L. The sponsor questioned the rationale for the reduction in CD4 counts and further stated that disclosure of CD4+ counts may be a sensitive issue. ATAGI considered the use of CD4 counts to determine the cohort of people living with HIV for funded RZV to be appropriate. The update of the definition for CD4 count for people with HIV was based on expert consensus within ATAGI to align with other international clinical case definitions for significant immunosuppression in people living with HIV generally being associated with a CD4 count <200/ μ L^{6,7} ATAGI considered CD4 counts as basic information all clinicians involved in the care of people living with HIV would have access to and/ or would measure. The ATAGI noted the CD4 count does not need to be revealed to receive RZV, or be recorded on the Australian Immunisation Register once administered.
- 3.33 Additionally, the sponsor proposed inclusion of a criteria (see circumstance (c) (iii) in paragraph 2.1 – ‘Vaccine may be provided to a person who (c) is at least 18 years of age and considered at increased risk of herpes zoster (iii) as determined by the treating physician to be at comparable risk to an individual in paragraph i’) to capture additional conditions or therapies that contain immunocompromised individuals who are at a similar level of risk as high or moderate risk groups currently not covered by the population level guidance provided by ATAGI, including combination therapies and immunomodulatory/immunosuppressive therapies which are not currently listed on the PBS. ATAGI does not agree to the proposal to allow NIP funded doses to be given based on clinician judgement as it would be subjective and may lead to substantial variation in practice and potentially result in use in a large cohort of people without significantly increased risk of HZ. ATAGI reiterated its previous advice that new medicines in each of the listed medication classes should automatically be considered as eligible for funded doses.

4 PBAC outcome

- 4.1 The PBAC recommended that varicella zoster virus recombinant vaccine (RZV) 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 18 years and older at a moderate to high risk of infection, as defined by the Australian Technical Advisory Group on Immunisation (ATAGI) in Table 1. The PBAC considered that RZV was likely to be cost effective at the requested cost per dose in the moderate (\$) and high risk populations (\$). The PBAC advised this cost per dose

⁶ <https://clinicalinfo.hiv.gov/en/glossary/aids-case-definition#:~:text=HIV%2FAIDS%20Glossary&text=Diagnostic%20criteria%20for%20AIDS%20established,an%20AIDS%2Ddefining%20condition>

⁷ https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1174008/Shingles_Green_Book_on_Immunisation_Chapter_28a_26_7_23.pdf

- only applied to individuals not currently covered on the National Immunisation Program (NIP).
- 4.2 The PBAC noted the consumer comments were supportive of expanding access to RZV on the NIP. Many of the comments noted the benefits of vaccinating immunocompromised individuals against HZ infection and described the effectiveness and safety of RZV in this population. The PBAC noted a majority of the populations considered to be at high risk of HZ infection (and referred to in the consumer comments) will be covered by this recommendation.
 - 4.3 The PBAC noted the ATAGI advice provided in September 2023 in response to the PBAC's March 2023 deferral for the broader population of immunocompromised individuals at increased risk of HZ infection. The PBAC noted the additional conditions and the immunosuppressive therapies (as outlined in Table 1) that conferred a moderate or high risk for HZ, both categories which ATAGI considered appropriate for funded vaccination with RZV. The PBAC noted the number of individuals within each of these populations (as outlined in Table 1) did not account for non-Indigenous individuals over 65 years of age and Aboriginal and Torres Strait Islander individuals over 50 years of age who are currently able to access RZV on the NIP.
 - 4.4 The PBAC noted the sponsor provided information to support the cost-effectiveness of RZV and associated financial implications based on the ATAGI advice. The PBAC noted the sponsor's estimated total number of moderate and high risk individuals eligible for vaccination was largely consistent with the ATAGI estimates with the exception of the inclusion of 40,000 to < 50,000 high risk individuals estimated to be on high dose methotrexate. The PBAC advised individuals on high dose MTX would largely be covered within other risk categories and it was not reasonable to include these additional 40,000 to < 50,000 individuals in the financial estimates.
 - 4.5 In addition to the high risk population defined by ATAGI, the PBAC noted the sponsor requested individuals on systemic corticosteroids and individuals aged 50 to 64 years of age with other conditions that confer a higher risk of HZ infection be included in the high risk cohorts. The PBAC noted the additional ATAGI advice that systemic corticosteroid use and some diseases (i.e., inflammatory bowel diseases and diabetes) alone should not be included in the high risk cohorts on the basis of uncertainty in the evidence of additional risk from corticosteroid use/disease alone. The PBAC noted many of these individuals were likely to access RZV via either the age or therapy criteria.
 - 4.6 The PBAC noted the sponsor stated that recommendations from the March 2023 PBAC meeting and July 2023 PBAC meeting were used as a frame of reference for cost-effectiveness within the proposed additional cohorts. The PBAC considered that, on balance, RZV was likely to be cost effective at the requested cost per dose in the moderate (\$) and high risk populations (\$). The PBAC advised this cost per dose only applied to individuals not currently covered on the NIP.

- 4.7 The PBAC considered RZV was not likely to be cost effective at the requested cost per dose (\$) in the low risk populations. The PBAC noted ATAGI advised this population was of a lower priority for funding.
- 4.8 The PBAC noted the sponsor stated the incremental impact of providing access to RZV on the NIP for moderate and high risk individuals (as defined by ATAGI) was an additional 200,000 to < 300,000 persons vaccinated, 300,000 to < 400,000 doses administered, and a cost to the NIP of \$60 million to < \$70 million. The PBAC noted this incremental cost was substantially overestimated for the reasons outlined in paragraph 3.26. The PBAC considered that, overall, the financial estimates provided by the sponsor were reasonable in the context of the overall cost of the program (approx. >\$1 billion) but advised it would be appropriate to revise the financials to only include individuals not currently covered on the NIP.
- 4.9 The PBAC advised that, based on advice from ATAGI, the following changes to the determination proposed by the sponsor were appropriate:
- Removal of the circumstances: “due to treatment with systemic corticosteroids (≥ 10 mg/day prednisolone equivalent dose) and considered by the treating physician to be at comparable risk to an individual in paragraph i” and “as determined by the treating physician to be at comparable risk to an individual in paragraph i”.
 - Amend the circumstance: “End stage renal disease/renal failure/chronic kidney disease on dialysis” to “Stage 5 kidney disease or on dialysis”.
- 4.10 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.

5 Recommended listing

5.1 Amend existing Determination as follows:

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	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 c. Those eligible populations who have received one dose privately can receive their second dose on the NIP

Circumstances

Vaccine may be provided to a person who:

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- (a) is at least 65 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 in subsection 7.

Subsection 7

For item 217A of Schedule 1, a designated vaccine in that item may be provided to a person who is at least 18 years of age who: and considered at increased risk of herpes zoster, i.e. individuals with:

- (a) has an underlying condition:
 - i. Acute haematological malignancies (acute leukaemia, aggressive lymphomas)
 - ii. Chronic haematological malignancies including myelodysplastic syndromes/chronic myeloproliferative disorders, lymphoproliferative malignancies and plasma cell dyscrasias e.g., myeloproliferative neoplasms, chronic lymphocytic leukaemia, indolent non-Hodgkin lymphoma, multiple myeloma
 - iii. Human immunodeficiency virus infection with CD4⁺ cell count < 200/ μ L
 - iv. Inborn errors of immunity with ongoing functional deficits including:
 - (A) humoral e.g., X-linked agammaglobulinemia
 - (B) combined defects e.g., severe combined immunodeficiency (SCID)
 - (C) phagocytic disorders e.g., chronic granulomatous disease (CGD)
 - (D) other inborn errors of immunity except complement disorders, hereditary angioedema (HAE) and IgA deficiency (considered lower risk).
 - v. Stage 5 kidney disease or on dialysis
- (b) malignancy, autoimmune or inflammatory conditions receiving immunomodulatory/immunosuppressive treatments including:
 - i. Cellular therapies (currently receiving or within the previous 24 months), including:
 - (A) autologous haematopoietic stem cell transplant
 - (B) allogeneic haematopoietic stem cell transplant (unless ongoing graft vs host disease with immunosuppressive therapy, where they remain at high risk beyond 24 months)
 - (C) chimeric antigen receptor T-cell therapy
 - ii. B and T-cell targeted monoclonal antibody therapies, currently or within the last 6 months, including:
 - (A) anti-CD20
 - (B) anti B-cell activating factor (BAFF)
 - (C) anti-CD52
 - (D) anti-thymocyte globulin
 - iii. Conventional chemotherapy for:
 - (A) treatment of haematological malignancy
 - (B) solid organ tumours, currently or within the last 6 months
 - iv. Immunosuppressive therapy to prevent organ rejection prior to or following solid organ transplantation, currently, or within the last 6 months
 - v. Conventional immunosuppressive agents currently or within the last 6 months, such as:
 - (A) high dose methotrexate \geq 20mg per week (oral and subcutaneous)
 - (B) azathioprine \geq 3.0mg/kg/day
 - (C) 6-mercaptopurine \geq 1.5mg/kg/day
 - (D) mycophenolate \geq 1g/day
 - (E) cyclophosphamide
 - (F) systemic calcineurin inhibitors (tacrolimus, cyclosporin)
 - (G) mTOR inhibitors
 - (H) purine analogues (cladribine)
 - vi. Biologic therapies (except lower risk biologics *) in the last 6 months, such as:
 - (A) tumour necrosis factor inhibitors (TNFi)
 - (B) T-cell co-stimulation modulators (e.g., Abatacept)
 - (C) soluble TNF receptors,
 - (D) type I interferon receptor inhibitors,
 - (E) proteasome inhibitors,
 - (F) interleukin (IL) inhibitors currently or within the last 6 months, including anti-IL1 antibodies, anti-IL4/13 antibodies, anti-IL5 antibodies, anti-IL6 antibodies, IL-6 receptor inhibitors

[^] anti-integrins e.g., natalizumab and vedolizumab, anti-IgE antibodies, anti-complement antibodies and lower risk IL inhibitors anti-IL17 antibodies, anti-IL 12/23 antibodies, anti-IL23 antibodies, and anti-IL31 antibodies

- vii. Immunomodulatory drugs including sphingosine-1-phosphate receptor modulators within the last 6 months
- viii. Oral small molecule targeted therapies, currently or within the last 6 months including: Bruton's tyrosine kinase (BTK) inhibitors, Janus kinase (JAK) inhibitors, BCR-ABL inhibitors

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.

6 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 latest information at any time.

7 Sponsor's Comment

GSK welcomes the PBAC recommendation to expand eligibility of Shingrix on the National Immunisation Program (NIP) for adults aged 18 years and older who are at increased risk of herpes zoster (shingles) due to specific underlying conditions and/or treatments.

We recognise and thank the medical societies, healthcare professionals, and patient organisations who provided advice and input about shingles and Shingrix on behalf of the communities they represent.

We acknowledge there remain Australians who are recommended by ATAGI to receive shingles vaccination but are not yet eligible for Shingrix under the NIP. We will continue to work to achieve equitable access to Shingrix for these groups of people.