7.03 RESPIRATORY SYNCYTIAL VIRUS VACCINE, Powder and suspension for injection (0.5 mL), Arexvy®, GLAXOSMITHKLINE AUSTRALIA PTY LTD.

1 Purpose of submission

1.1 The standard re-entry resubmission requested National Immunisation Program (NIP) listing of a recombinant respiratory syncytial virus (RSV) pre-fusion F protein 3 older adult (RSVPreF3 OA) vaccine for the prevention of RSV-confirmed lower respiratory tract disease (LRTD) among adults aged ≥75 years of age (YOA) and Aboriginal and Torres Strait Islander people aged 60-74.

1.2 The Australian Technical Advisory Group on Immunisation (ATAGI) (at the PBAC's July 2024 consideration of RSVPreF3 OA) and the Australian Immunisation Handbook (AIH) have supported use of RSVPreF3 OA in three populations: patients aged 75 years and over; Aboriginal and Torres Strait Islander people aged 60 to 74 years; and people aged 60 to 74 years with conditions that increase their risk of severe disease due to RSV (paragraph 7.1, RSVPreF3 OA Public Summary Document [PSD], July 2024). However, the resubmission requested listing for the first two groups only, stating that the third group would be addressed in a subsequent resubmission.

1.3 Listing was requested on the basis of a cost-utility analysis (CUA) versus no vaccine. The key components of the clinical issues addressed by the resubmission are presented in Table 1.

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

Component	Description
Target NIP Population	Adults ≥75 YOA Aboriginal and Torres Strait Islander adults 60-74 YOA[a]
Intervention	RSVPreF3 OA vaccine, single dose
Comparator	Main comparator: no vaccine Near market comparator: RSVpreF
Outcomes	Primary efficacy: single dose during first season – prevention of RSV-confirmed LRTD Secondary efficacy: cumulative efficacy of a single dose over 3 RSV seasons - prevention of RSV-confirmed LRTD Secondary safety: solicited (subset) and unsolicited AEs, all SAEs and pIMDs
Clinical claim	RSVPreF3 OA vs no vaccine (direct comparison): superior efficacy and a similar safety profile, despite being more reactogenic than placebo. RSVPreF3 OA versus RSVPreF: • RSVPreF3 OA has demonstrated durable and clinically meaningful efficacy over 3 complete RSV seasons; • RSVpreF has demonstrated durable and clinically meaningful efficacy over 2 complete RSV seasons; • similar safety profile.

Source: Table 1-3, p27 of the resubmission.
AE = adverse event; LRTD = lower respiratory tract disease; pIMD = potential immune mediated disorder; RSV = respiratory syncytial virus; RSVPreF = RSV pre-fusion protein; RSVPreF3 OA= RSV pre-fusion protein 3 older adult; SAE = serious adverse event; YOA = years of age.
[a] Listing for use in the Aboriginal and Torres Strait Islander population was previously considered by the PBAC, but not explicitly requested (paragraph 3.1, RSVPreF3 OA PSD, July 2024)
Blue shading indicates data previously seen by the PBAC.

2 Background

Registration status

2.1 RSVPreF3 OA was approved by the Therapeutic Goods Administration (TGA) on 14 January 2024 for the active immunisation of individuals 60 years and older for the prevention of LRTD caused by RSV. From 31 March 2025, the TGA-registered indication was expanded to include adults aged 50-59 who are at increased risk for RSV disease.

2.2 The pre-PBAC response stated that no submissions have been made to the TGA requesting a decision on the timing of revaccination and described the relevant ongoing trials with revaccination data (see paragraph 3.3 below).

Previous PBAC consideration

2.3 A submission for RSVPreF3 OA was considered by the PBAC in July 2024 and not recommended. The key matters of concern from the July 2024 submission are summarised in Table 2.

Table 2: Summary of key matters of concern

Component	RSVPreF3 OA PSD: July 2024	How the resubmission addressed it
Target NIP Population	Two alternative schedules were proposed: (i) ≥60 YOA; (ii) ≥75 YOA.	Two populations were proposed, consistent with the two populations recommended by the PBAC in November 2024 for RSVpreF: ≥75 YOA adults; and 60-74 YOA First Nations adults.

Component	RSVPreF3 OA PSD: July 2024	How the resubmission addressed it
	The PBAC considered it was inappropriate to exclude high risk patients ≥60 with a clinical need (paragraph 7.9, RSVPreF3 OA PSD, July 2024).	The resubmission stated that the third group recommended by ATAGI (high risk patients ≥60) would be addressed in a subsequent resubmission.
Clinical evaluation	The PBAC noted that further results from AReSVi-006 and RSV OA=ADJ-004 were expected in September 2024 and would provide further information regarding the appropriate timing of revaccination (paragraph 7.10, RSVPreF3 OA PSD, July 2024)	Updated results from AReSVi-006 presented in the resubmission do not provide evidence for appropriate timing of revaccination. The resubmission did not include a claim for revaccination or a proposed revaccination schedule. Updated data from the RSV OA=ADJ-004 immunogenicity trial (36/37 Month analysis) demonstrated a robust humoral and cellular immune response with a single dose of RSVPreF3 OA 36 months after vaccination, with a slower decline of neutralising antibody titres between 24 and 36 months compared with the first 24 months. In the ongoing pivotal immunogenicity trial, RSV OA=ADJ-004, and a new crossover and revaccination extension of RSV OA=ADJ-006 (RSV OA=ADJ-012, NCT06534892), immune persistence of a single dose of RSVPreF3 OA and alternate revaccination schedules will be assessed up to Month 60 after initial vaccination (results not yet available).
Economic model		
Modelled populations	CEAs for use in higher risk individuals and Aboriginal and Torres Strait Islander people 60-74 YOA were not presented (paragraph 6.45, RSVPreF3 OA PSD, July 2024).	The resubmission presented a CEA for Aboriginal and Torres Strait Islander people 60-74 YOA while noting that the 60-74 at-risk population will be submitted for consideration at a future PBAC meeting.
Vaccine efficacy/duration of protection	Limited data (18-month median follow-up) were available to estimate the duration of protection of RSVPreF3 OA over a 3-year period (paragraph 6.88, RSVPreF3 OA PSD, July 2024).	The resubmission presented an updated analysis based on the end of season 3 analysis with extended median of 30.6-month follow-up.
Vaccination month	March as the vaccination month unlikely reflected in practice (paragraph 6.51, RSVPreF3 OA PSD, July 2024).	The resubmission assumed vaccination can occur at any time during the year, reflecting the ESC and the ATAGI advice (ATAGI advice, March 2025).
Hospitalisation rates	Likely overestimated RSV-associated hospitalisation rate (paragraph 6.55, RSVPreF3 OA PSD, July 2024). This was primarily due to the overestimated unadjusted rates from Branche et al. 2021 presenting data from a densely populated area with different testing practices to the Australian setting.	Not addressed in the resubmission. The revised rates were inconsistent with the ATAGI Advice (see paragraphs 6.60 to 6.64).
Hospitalisation costs	Overestimated RSV-associated hospitalisation costs (paragraph 6.88, RSVPreF3 OA PSD, July 2024), primarily due to unnecessary adjustment for LOS to the NEP cost weight (paragraph 6.65, RSVPreF3 OA PSD, July 2024).	The resubmission presented revised RSV-associated hospitalisation costs based on an Australian study on non-Covid viral pneumonia (Hitch et al. 2024). The revised costs were comparable to the estimates in the previous submission and remained higher than the costs previously considered reasonable by the PBAC (see paragraph 6.66).

Component	RSVPreF3 OA PSD: July 2024	How the resubmission addressed it
Administration cost	Administration costs not included (paragraph 6.88, RSVPreF3 OA PSD, July 2024).	The resubmission included administration costs equal to MBS Item 3, assuming 50% co-vaccination. The PSCR revised this to 36% of an MBS Item 3, consistent with the PBAC's advice for RSVpreF in November 2024.
Presenting the results in age bands	A strong age gradient for vaccine cost-effectiveness and presenting the results in age bands required (paragraph 6.88, RSVPreF3 OA PSD, July 2024).	The submission presented results per age group (in 5 year bands) for the economic evaluations for ≥75 YOA. The ESC considered this issue was less pertinent given the submission did not request listing in the 60–74 YOA at-risk population.
Revaccination	Present information available regarding the need for revaccination, and if relevant include revaccination in the economic model required (paragraph 6.88, 7.21, RSVPreF3 OA PSD, July 2024).	The resubmission noted that the need and timing of revaccination was not yet established. No revaccination was proposed in the resubmission.

Source: Complied during the evaluation; Table 3-1, p166 of the resubmission.
ATAGI = Australian Technical Advisory Group on Immunisation; CEA = cost-effectiveness analysis; ESC = Economic Sub Committee; LOS = length of stay; LRTD = lower respiratory tract disease; MBS = Medicare Benefits Schedule; NEP = National Efficient Price; OA = older adults; PBAC = Pharmaceutical Benefits Advisory Committee; PSCR = Pre-Sub-Committee Response; PSD = Public Summary Document; RSV = respiratory syncytial virus; RSVPreF3 OA = RSV pre-fusion protein 3 older adult; TGA = Therapeutic Goods Administration; VE = vaccine efficacy; YOA = years of age.

2.4 RSVPreF3 OA was considered and not recommended by the PBAC at the July 2024 meeting for two alternative populations (i) adults aged ≥60 YOA; and (ii) adults ≥75 YOA. In July 2024, the PBAC considered:

- RSVPreF3 OA was superior in effectiveness against no vaccine in adults ≥60 YOA over 2 RSV seasons (paragraphs 7.12 and 7.13, RSVPreF3 OA PSD, July 2024).
- The incremental cost-effectiveness ratio (ICER) was unacceptably high and uncertain for both populations proposed by the submission at the proposed price (paragraph 7.17, RSVPreF3 OA PSD, July 2024). The PBAC noted that the ICER increased to over $55,000 to < $75,000/QALY for ≥60 YOA and over $25,000 to < $35,000/QALY for ≥75 YOA (paragraph 7.17, RSVPreF3 OA PSD, July 2024) using a multivariate sensitivity analysis that assumed vaccine efficacy (VE) over 2 years (using VE analysis 4, which corresponded to a median follow-up of 23.3 months), and a reduced hospitalisation cost (using unadjusted NHCDC cost weights hospitalisation costs).
- The cost-effectiveness of RSVPreF3 OA in Aboriginal and Torres Strait Islander people aged 60-74 years, and high risk people aged 60-74 years, was unknown as this was not addressed by the submission (paragraph 7.1, RSVPreF3 OA PSD, July 2024).

2.5 The PBAC considered an application for RSVPreF (Abrysvo) in older adults, the proposed near market comparator, at its November 2024 PBAC meeting. It recommended NIP listing for adults aged ≥75 years and for Aboriginal and Torres Strait Islander people aged 60–74 years. However, it did not support listing for adults aged 60–74 at high risk of severe RSV disease. This exclusion was due to concerns that the economic evaluation lacked a robust estimate of cost-effectiveness, with baseline

risks and benefits unclear and likely overestimated. While the PBAC acknowledged the vaccine's superiority over no vaccine in terms of effectiveness and its acceptable safety profile, it noted uncertainty around the magnitude and duration of protection in the proposed populations. The cost-effectiveness analysis was to be revised to achieve an ICER between $5,000 and <$15,000 per QALY gained for both the (i) ≥75 YOA; and (ii) Aboriginal and Torres Strait Islander people aged 60–74 years populations (paragraphs 7.1, 7.17 and 7.19, RSVPreF PSD, November 2024). The PBAC noted that listing was requested for a single dose and that the need for revaccination was unknown (paragraph 7.9, RSVPreF PSD, November 2024).

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

ATAGI advice

2.6 The Australian Technical Advisory Group on Immunisation (ATAGI) provided pre-submission advice for the PBAC to consider for this resubmission, dated 7 March 2025. The ATAGI previously provided advice for the RSVPreF3 OA submission considered at the July 2024 PBAC meeting, including pre-submission advice dated 21 December 2023, and post-submission advice dated 2 May 2024.

3 Requested listing

MEDICINAL PRODUCT	NIP price	Available brands
Recombinant Respiratory Syncytial Virus (RSV) pre-fusion F protein 3 older adult vaccine, 120 mcg powder vial and suspension vial[a]	$[redacted] PSCR: $[redacted] Pre-PBAC: $[redacted]	Arexvy
National immunisation program • ≥ 75 years of age • Aboriginal and Torres Strait Islander people aged 60-74 Duration of listing: ongoing NIP cohort		

Source: Compiled during the evaluation from Tables 1-10 p40 and 3-10 p164 of the resubmission.
NIP = National Immunisation Program; RSV = respiratory syncytial virus.
a. The PSCR and pre-PBAC response stated that GSK intends to transition from a vial-vial formulation to vial-prefilled syringe formulation.
Blue shading indicates data information seen by the PBAC.

3.1 The resubmission proposed a price of $[redacted], reduced from the July 2024 submission price of $[redacted] per vial. The Pre-Sub-Committee Response (PSCR) and pre-PBAC response offered prices of $[redacted] per vial, and $[redacted] per vial, respectively.

3.2 The Australian Immunisation Handbook (AIH) recommends that RSV vaccines may be given at any time of the year but, where possible, should be offered before the start of the RSV season. The ATAGI stated that, ideally, vaccination would occur prior to the RSV season (if living in an area of seasonality), however, it supported a year-round program (ATAGI advice March 2025).

3.3 The resubmission requested NIP listing of a single dose of RSVPreF3 OA per lifetime, and stated that the need for revaccination was yet to be established. Optimal timing for potential revaccination will be informed by two trials that are ongoing: the pivotal

immunogenicity trial, RSV OA=ADJ-004 and a new crossover and revaccination extension of AreSVi-006 (RSV OA=ADJ-012, NCT06534892). Immune persistence of a single dose of RSVPreF3 OA and alternate revaccination schedules will be assessed up to Month 60 after initial vaccination. As such, there is the possibility of a request for NIP listing of a revaccination in the future.

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

4 Population and disease

4.1 RSV is highly infectious and spreads via respiratory droplets. Most patients develop signs of upper respiratory tract disease (URTD), which in some patients progresses to the lower respiratory tract leading to symptoms such as cough, wheezing, and shortness of breath. Severe RSV may require hospitalisation, including admission into intensive care units (ICU), and/or receiving mechanical ventilation. Aboriginal and Torres Strait Islander people have a greater risk of RSV hospitalisation compared with non-Indigenous Australians.

4.2 RSV became a notifiable disease in Australia in July 2021, and the burden in older patients is only recently emerging. The resubmission stated that diagnosis of RSV infection in Australian older adults has been systematically underestimated due to low disease awareness, lack of mandatory reporting of RSV cases in many Australia jurisdictions until June 2022, low rates of routine RSV testing, and low sensitivity of the standard method used for RSV testing. After adjusting for underestimation, the resubmission estimated an annual incidence of 3.94 symptomatic RSV infections per 100 people and 12,769 RSV-associated hospitalisations in adults ≥75 years. However, the evaluation considered that the resubmission may have overestimated RSV incidence. Recent published data from Western Australia reported an incidence rate of 0.2 per 100 in adults aged ≥75 years[1]. While this figure may underestimate the true burden, as it covers the period from 2017 to 2023 (with mandatory RSV notification having been introduced gradually from mid-2021), the evaluation considered it may not be plausible for the incidence rate estimated in the resubmission (3.94%) to be nearly 20 times higher than that reported in the most recent Australian study. Australian Institute of Health and Welfare (AIHW) data show that, pre-COVID-19, there was an increasing trend in hospitalisations resulting in a substantial burden in adults aged ≥80 years, with a lesser but still notable impact in adults ≥75 years.[2]

4.3 There are currently no vaccines funded on the NIP for RSV-related disease in older adults, however RSVPreF3 OA (Arexvy) and RSVPreF (Abrysvo) are available via private

[1] Foley, D.A.; Minney-Smith, C.A.; Tjea, A.; Nicol, M.P.; Levy, A.; Moore, H.C.; Blyth, C.C. The Changing Detection Rate of Respiratory Syncytial Virus in Adults in Western Australia between 2017 and 2023. *Viruses* 2024, *16*, 656. https://doi.org/10.3390/v16050656

[2] AIHW data analysis conducted by the NCIRS (https://ncirs.org.au/ncirs-webinar-series/07032024-rsv-vaccines-protection-older-adults)

prescription.

4.4 RSVPreF3 OA is a combination of the RSVPreF3 antigen and the $AS01_E$ adjuvant system. RSVPreF3 OA was designed to induce a humoral and cellular immune response, to help protect older adults from RSV infection, including those with underlying co-morbidities.

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

5 Comparator

5.1 The resubmission nominated 'no vaccine' as the main comparator. The evaluation considered that this was reasonable, and noted it was consistent with the PBAC's previous advice (paragraph 7.11, RSVPreF3 OA PSD, July 2024).

5.2 The resubmission nominated RSVPreF (Abrysvo) as a near market comparator. The evaluation considered that this was appropriate. RSVPreF is TGA approved and was recommended by the PBAC for the same two populations for which RSVPreF3 OA listing is being sought (paragraph 7.1, RSVPreF PSD, November 2024), however it has not yet been listed on the NIP.

5.3 The PBAC considered that RSVPreF was the main comparator as it was recommended for NIP listing at the November 2024 PBAC meeting.

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

6 Consideration of the evidence

Sponsor hearing

6.1 The sponsor provided a recorded hearing for this item.

6.2 The clinician, a specialist in geriatric medicine with a major interest in immunisation, discussed the clinical manifestations of RSV in older adults, highlighting serious complications associated with infection including frailty, hospitalisation, intensive care admission, loss of function, or death, particularly in people aged over 60 years, and even more so in those aged over 75 years. In addition to a significant number of hospitalisations of older Australians each year due to RSV infection, the clinician described longer term effects, such as being unable to work or live independently and reduced quality of life. The clinician emphasised the importance of a vaccination program via the NIP and described the success observed in the US and UK from real world evidence that showed a decline in hospitalisations with RSV vaccination. The clinician discussed the efficacy of the RSVPreF3 OA vaccine over 3 seasons and described a favourable safety profile. Finally, the clinician referred to the preference for preventing rather than treating disease, and the flow on effects in terms of reducing burden on the healthcare system.

6.3 The PBAC considered that the hearing was informative, as it provided a clinical perspective on the benefits of preventing RSV infection.

Consumer comments

6.4 The PBAC noted and welcomed the input from individuals (12), health care professionals (17) and organisations (8) via the Consumer Comments facility on the PBS website, supporting the NIP listing of RSVPreF3 OA for prevention of LRTD caused by RSV in older Australians.

6.5 Two medical organisations (the Royal Melbourne Hospital and the Australasian Society of Clinical Immunology and Allergy [ASCIA]) indicated their support for the NIP listing by describing vaccination for RSV as a critical element in preventing infectious diseases and associated hospitalisations, especially in immunocompromised patients and those with chronic medical conditions.

6.6 Similarly, six consumer groups urged the PBAC to recommend listing on the NIP. Hearts4heart highlighted the burden of RSV disease in older adults, especially in patients with chronic co-morbidities, and stated that it is underestimated and under-diagnosed. It noted the increasing hospitalisation rates from RSV infection with increasing age of patients. It also noted the significant impact of RSV disease on healthcare systems in terms of increased healthcare utilisation and economic burden. In addition to the above-mentioned topics, the Immunisation Foundation of Australia emphasised the requirement for equitable protection from RSV for older Australians. Cystic Fibrosis Queensland described the advantages of immunisation with RSVPreF3 OA for people with cystic fibrosis and lung transplant recipients. Asthma Australia described the negative effects of RSV infection in older Australians with asthma, noting that viral respiratory infections are the most common trigger for asthma exacerbations. Lung Foundation Australia described the strong community support for access to a vaccine for RSV on the NIP, noting the serious consequences of contracting the disease and the prohibitive cost for an older population. Kidney Health Australia described the importance of people with kidney failure having access to vaccines such as that for RSV, including First Nations Australians who are disproportionately impacted by chronic kidney disease.

6.7 As well as noting several of the topics discussed above, the health care professionals (HCPs) commented on individuals experiencing adverse effects for a long period of time following RSV infection, especially in high-risk cohorts such as older people. The HCPs described the impact of vaccination as having many benefits that would apply to the older Australian population, including reduced mortality and hospitalisation, reduced long-term morbidity/frailty, and increased independence.

6.8 The individuals who commented comprised an individual that had been vaccinated with RSVPreF3 OA, those who would like to be vaccinated (6), a parent/partner of a current/potential vaccinated individual (3), and other interested individuals (2). The consumer input described an out-of-pocket cost of more than $300 to receive RSV vaccination as difficult to afford, leaving elderly patients with underlying risk factors vulnerable to preventable health outcomes.

6.9 The PBAC recalled it had previously considered input in support of NIP listing of the vaccine as summarised in the July 2024 PSD for RSVPreF3 OA (paragraphs 6.2 to 6.6).

6.10 The PBAC noted that the consumer comments consistently supported the proposed NIP listing in adults aged ≥75 years of age and Aboriginal and Torres Strait Islander people aged 60-74. In addition, some of the comments highlighted the ATAGI advice which also recommends RSV vaccine for adults ≥60 years with medical conditions that increase their risk of severe disease, and asked the PBAC to consider extending the NIP populations to include this group, noting these patients have a greater risk of being hospitalised from RSV compared with those without these conditions.

Clinical trials

6.11 The resubmission was based on the same trial for RSVPreF3 OA as presented in the July 2024 submission, AReSVi-006. The key head-to-head randomised trial compared RSVPreF3 OA (N = 12,469) to placebo (N = 12,503). The resubmission presented updated results up to 30.6 months of median follow-up (from 17.8 months at the end of Season 2 presented in the July 2024 submission) corresponding to 3 complete RSV seasons in the northern hemisphere (NH) in adults ≥60 YOA, across different RSV subtypes, age groups and comorbidity categories.

6.12 A claim of superiority was made for VE based on the results from AReSVi-006 in terms of prevention of first occurrence of reverse transcription-polymerase chain reaction (RT-PCR) confirmed RSV-associated LRTD in adults ≥60 YOA, with an acceptable safety profile relative to placebo. The submission presented a pre-specified subgroup analysis of individuals aged 70-79 to support the requested listing in adults ≥75 YOA.

6.13 No evidence for Aboriginal and Torres Strait Islander people was available from the AReSVi-006 trial. The submission addressed this lack of data by using multipliers in the economic analysis to account for the anticipated higher incidence of RSV among Aboriginal and Torres Strait Islander people.

6.14 ATAGI stated that RSVPreF3 OA was effective in adults ≥60 YOA, inclusive of the proposed NIP populations, Aboriginal and Torres Strait Islander people aged 60-74 and adults ≥75 years, although efficacy beyond 3 seasons, and the need for further vaccination, remains unknown (ATAGI advice, March 2025).

6.15 The resubmission presented updated immunogenicity and safety results at Month 36/37 in adults ≥60 YOA from one supportive trial, RSV OA=ADJ-004. In its July 2024 consideration, the PBAC had considered immunogenicity data up to 24 months post Dose 1 (paragraph 6.22, RSVPreF3 OA PSD, July 2024).

6.16 Details of the trials presented in the resubmission are provided in Table 3.

Table 3: Trials and associated reports presented in the resubmission

Trial ID	Protocol title/ Publication title	Publication citation
Pivotal efficacy trial		
AReSVi-006 (NCT04886596)	A phase 3, randomized, placebo-controlled, observer-blind, multi-country study to demonstrate the efficacy of a single dose and annual revaccination doses of GSK's RSVPreF3 OA investigational vaccine in adults aged 60 years and above. VE analysis 1 (Interim Season 1 Analysis)	Clinical Study Report
	Papi A, Ison, MG, Langley, JM et al. Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults	NEJM 2023, 388: 595-608. DOI: 10.1056/NEJMoa2209604
	Phase 3, randomized, placebo-controlled, observer blind, multi-country study to demonstrate the efficacy of a single dose and annual revaccination of GSK's RSVPreF3 OA investigational vaccine in adults aged 60 years and above (End of Study CSR).	Clinical Study Report, 9 September 2024
	Analysis: VE Analysis 3 (End of Season 2 Analysis) Study report number: 212494	Clinical Study Report
	Ison MG, Papi A, Athan, E et al. Efficacy and safety of respiratory syncytial virus prefusion F protein vaccine (RSVPreF3 OA) in older adults over 2 RSV seasons.	Clinical Infectious Diseases 2024, ciae010. doi: 10.1093/cid/ciae010.
	Feldman, RG, Antonelli-Incalzi, R, Steenackers, K. et al. Respiratory syncytial virus prefusion F protein vaccine is efficacious in older adults with underlying medical conditions.	Clinical Infectious Disease 2023; ciad471. DOI: 10.1093/cid/ciad471
	Curran D., Matthews S., Cabrera E.S. et al. The respiratory syncytial virus prefusion F protein vaccine attenuates the severity of respiratory syncytial virus-associated disease in breakthrough infections in adults ≥ 60 years of age.	Influenza and Other Respiratory Viruses 18.2 (2024): e13236. DOI: 10.1111/irv.13236
	Ison MG, Papi A, Athan E et al. Efficacy, safety, and immunogenicity of the AS01E-adjuvanted respiratory syncytial virus 3 prefusion F protein vaccine (RSVPreF3 OA) in older adults over three RSV seasons: a randomized trial.	Pre-print publication
Immunogenicity trial		
RSV OA=ADJ-004 (NCT04732871)	A phase 3, randomized, open-label, multi-country study to evaluate the immunogenicity, safety, reactogenicity and persistence of a single dose of the RSVPreF3 OA investigational vaccine and different revaccination schedules in adults aged 60 years and above Analysis: Month 37 analysis (1 month post 36-month revaccination)	Clinical Study Report
	Schwarz, TF, Hwang, SJ, Ylisastigui, P. et al. Immunogenicity and safety following one dose of AS01$_E$-adjuvanted respiratory syncytial virus prefusion F protein vaccine in older adults: a phase 3 trial. Schwarz, TF, Hwang, SJ, Ylisastigui, P. et al. Immunogenicity and safety of a second dose of the respiratory syncytial virus (RSV) prefusion F protein vaccine (RSVPreF3 OA), 12 months after the first dose in adults ≥ 60 years.	JID 2023; jiad546. DOI: 10.1093/infdis/jiad546 The Ninth ESWI Influenza Conference Valencia. Page 285-286.

Source: Table 2-6, p53-54 of the resubmission.
RSVPreF3 OA = Recombinant Respiratory Syncytial Virus (RSV) pre-fusion F protein 3 older adult.
Blue shading indicates studies previously seen by the PBAC.

6.17 The key features of the direct randomised trial are summarised in Table 4.

6.18 AReSVi-006 was initially designed to assess the efficacy of RSVPreF3 OA against RSV-related LRTD following different dosing schedules: a single dose of vaccine up to the end of Season 3 in the Northern Hemisphere (NH) or following an annual

revaccination schedule at 12- and 24-months post Dose 1 administration. However, the trial protocol was amended on 31 October 2023 to remove the Month 24 revaccination dose schedule because initial analysis of efficacy for the 12-month revaccination dose demonstrated no additional efficacy benefit for the trial population. The resubmission noted that 5,742 participants (RSVPreF3 OA: 1,406 participants; placebo: 4,333 participants) from the NH received their second annual revaccination dose at Month 24 (Dose 3) as this occurred before the approval of the protocol amendment. These participants were included in the updated safety results and censored from some of the VE analyses. The trial results presented in the comparative effectiveness section reflect efficacy of a single dose of RSVPreF3 OA.

Table 4: Key features of the included evidence

Trial	N	Design/ duration	Risk of bias	Patient population	Outcomes	Use in modelled evaluation
RSVPreF3 OA versus placebo						
AReSVi-006	24,966[a]	Phase 3 R, OB, PC, MC Completed	Low	Adults ≥60 YOA	Primary outcome: reduction of the risk of the first occurrence of RT-PCR confirmed RSV-LRTD Key secondary outcomes: safety, PROs	Reduction of the risk of the first occurrence of RT-PCR confirmed RSV-LRTD, safety

Source: Compiled during the evaluation from Table 2-7, pp66-67 and Table 2-10, p73 of the submission.
MC = multi-centre; OB = observer blinded; PC = placebo-controlled; PRO = patient reported outcome; R = randomised; RSV-LRTD = lower respiratory tract disease respiratory syncytial virus; RT-PCR = reverse transcription-polymerase chain reaction.
[a] Population corresponds to the modified exposed set (mES) which excludes individuals who develop RSV-ARI before Day 15 post first dose (1 in the RSVPreF3 OA arm and 5 in the placebo arm).
Blue shading indicates information previously seen by the PBAC.

6.19 AReSVi-006 recruited adults ≥60 YOA at the time of first vaccination, which is broader than the NIP target population proposed in the resubmission; participants aged >70 YOA formed 44.2% of the full study population.

6.20 The resubmission presented an unadjusted unanchored indirect comparison (hereafter, indirect treatment comparison (ITC)) of RSVPreF3 OA (pivotal trial; AreSVi-006) with RSVPreF (pivotal trial; RENOIR).

Comparative effectiveness

RSVPreF3 OA (Arexvy) versus placebo

6.21 The primary VE outcome was assessed at the end of Season 1 (median follow-up 6.7 months) and was previously considered by the PBAC (RSVPreF3 OA PSD, July 2024). The updated follow-up cumulative VE results for the prevention of RSV-LRTD are presented in Table 5. The resubmission stated that the VE of RSVPreF3 OA against the proposed primary and secondary outcomes was demonstrated if the lower limit of the two-sided confidence interval (CI) was above the pre-defined threshold of 20%. The End of Study CSR stated that the 20% lower limit of the 2-sided CI applied over several seasons; therefore the evaluation considered that the same threshold applied to the interpretation of secondary endpoints (i.e., cumulative vaccine efficacy).

6.22 The results for AReSVi-006 were based on the pre-specified analysis that included RSV season as a covariate to account for differences between seasons in RSV-LRTD incidence rates, efficacy, follow-up time, or group sizes.

Table 5: Cumulative VE against first occurrence of RSV-LRTD, in participants ≥ 60 YOA (single dose, mES population and with season as a covariate)

Endpoint	RSVPreF3 OA				Placebo				VE % % CI [a]; p-value
	N	n	T (year)	n/T (per 1000)	N	n	T (year)	n/T (per 1000)	
VE for the prevention of RSV-LRTD									
Over Season 1[b] (FUP 6.7 m) – NH	12,466	7	6,865.9	1.0	12,494	40	6,857.3	5.8	**82.58 (57.89, 94.08) <0.0001**
Over Season 1 & 2[b] (FUP 17.8 m) – NH	12,469	30	14,662.6	2.0	12,498	139	17,269.0	8.0	**67.18 (48.19, 80.04; <0.0001)**
Over Season 1, 2 & 3[b] (FUP 30.6 m) – NH	12,468	48	19,748.8	2.4	12,498	215	27,363.6	7.9	**62.91 (46.74, 74.79; <0.0001)**

Source = Table 2-19 and Table 2-20, p90 and p92 of the resubmission.
CI = confidence interval; FUP = follow up; m = months; mES = modified exposed set; N = number of participants; n = number of participants with at least one RT-PCR confirmed RSV case; n/T (per 1000) = incidence rate of participants reporting at least one event; NH = northern hemisphere; RSVPreF3 OA= RSV pre-fusion protein 3 older adult; T (year) = sum of follow-up time (from Day 15 post-vaccination till first occurrence of the event or till the efficacy data lock point or till drop-out date) expressed in years; VE = vaccine efficacy (Poisson method – adjusted by age, region and season).
[a] 96.95% CI for primary endpoint (RSV-LRTD, end of Season 1 in NH); 97.5% CI for confirmatory secondary endpoint (RSV-LRTD, season 1 + 2 and season 1 + 2 + 3)
[b] Primary outcome defined as reduction of the risk of the first occurrence of RT-PCR confirmed RSV-LRTD.
Bold text indicates statistically significant result.
Blue shading indicates information previously seen by the PBAC.

6.23 Over 3 RSV seasons, the cumulative VE of a single dose of RSVPreF3 OA against first occurrence of RT-PCR-confirmed RSV-LRTD was 62.91% (97.5% CI: 46.74, 74.79). As the lower bound of the CI was >20%, the predefined success criteria for the prevention of LRTD-RSV over several seasons, the confirmatory secondary objective was demonstrated (Table 5). Based on the updated clinical evidence, ATAGI stated that RSVPreF3 OA provides effective prevention for RSV for at least 3 RSV seasons in adults ≥60 YOA, inclusive of the nominated target populations (adults ≥75 YOA; adults with at least one risk factor ≥60 YOA; Aboriginal and Torres Strait Islander people ≥60 YOA). The evaluation noted that the cumulative VE estimates over a period of 3 RSV seasons were lower than those reported in Season 1 and over 2 seasons. The PBAC previously considered that RSVPreF3 OA was effective and superior compared to placebo in adults ≥60 YOA, inclusive of those ≥75 YOA. However, it noted uncertainty around the magnitude and duration of benefit given that VE waned as the duration of follow up increased (paragraph 6.42, RSVPreF3 OA PSD, July 2024). VE waning was confirmed in the updated results, where cumulative VE fell from 67.18% (over 2 seasons) to 62.91% (over 3 seasons). Efficacy beyond 3 seasons, and the timing for further vaccination, remains unknown (ATAGI advice, March 2025).

6.24 Cumulative VE by RSV subtype and against severe RSV and RSV-ARI for end of Season 3 is presented in Table 6.

Table 6: Cumulative VE against the first occurrence of RSV-LRTD by RSV type, severe RSV-LRTD, and RSV-ARI, in participants ≥60 YOA (single dose, mES population, with season as a covariate)

Endpoint	RSVPreF3 OA				Placebo				VE % (95% CI); p-value
	N	n	T (year)	n/T (per 1000)	N	n	T (year)	n/T (per 1000)	
VE for the prevention of RSV-LRTD by RSV type									
Over Season 1 & 2 RSV-A (FUP 17.8 m)	12,469	6	14,673.7	0.4	12,498	48	17,323.5	2.8	**80.46 (53.95, 93.20); <0.0001**
Over Season 1 & 2 RSV-B (FUP 17.8 m)	12,469	24	14,665.5	1.6	12,498	90	17,297.6	5.2	**59.66 (35.80, 75.54); <0.0001**
Over Season 1, 2 & 3 RSV-A (FUP 30.6 m)	12,468	14	19,780.8	0.7	12,498	80	27,524.6	2.9	**69.83 (42.18, 85.72); <0.0001**
Over Season 1, 2 & 3 RSV-B (FUP 30.6 m)	12,468	34	19,760.3	1.7	12,498	135	27,454.0	4.9	**58.57 (35.90, 74.11); <0.0001**
VE for the prevention of severe-RSV LRTD (any 'severe' definition) [a]									
Over Season 1 (FUP 6.7 m)	12,466	1	6,867.9	0.1	12,494	17	6,867.7	2.5	**94.10 (62.37, 99.86); 0.0001**
Over Season 1 & 2 (FUP 17.8 m)	12,469	7	14,672.6	0.5	12,498	48	17,320.6	2.8	**78.83 (52.59, 91.96); <0.0001**
Over Season 1, 2 & 3 (FUP 30.6 m)	12,468	15	19,778.4	0.8	12,498	75	27,526.4	2.7	**67.38 (42.43, 82.68); <0.0001**
VE for the prevention of RSV-ARI									
Over Season 1 (FUP 6.7 m)	12,466	27	6,858.7	3.9	12,494	95	6,837.8	13.9	**71.71 (56.23, 82.27); <0.0001**
Over Season 1 & 2 (FUP 17.8 m)	12,469	94	14,626.4	6.4	12,498	292	17,167.0	17.0	**52.74 (40.01, 63.04); <0.0001**
Over Season 1, 2 & 3 (FUP 30.6 m)	12,468	131	19,654.5	6.7	12,498	428	27,086.0	15.8	**51.13 (40.31, 60.21); <0.0001**

Source: Table 2-21, 93 and Tables 2-23, 2-24, 2-25, p96-98 of the resubmission.

CI = confidence interval; FUP = follow up; m = months; mES = modified exposed set; N = number of participants; n = number of participants with at least one RT-PCR confirmed RSV case; n/T (per 1000) = incidence rate of participants reporting at least one event; RSVPreF3 OA= RSV pre-fusion protein 3 older adult; T (year) = sum of follow-up time (from Day 15 post-vaccination till first occurrence of the event or till the efficacy data lock point or till drop-out date) expressed in years; VE = vaccine efficacy (Poisson method – adjusted by age, region and season).

[a] Results for severity include those that apply to any of the two severity definitions used in AReSVi-006.

Bold text indicates statistically significant result.

Blue shading indicates results previously seen by the PBAC.

6.25 Given the lower bound of the 95% CI exceeded 20%, the cumulative VE was demonstrated over 3 RSV seasons for the prevention of severe RSV-LRTD (67.38%; 95% CI: 42.43, 82.68), and RSV-ARI (51.13%; 95% CI: 40.31, 60.21). The cumulative VE was also demonstrated over 3 RSV seasons with respect to RSV sub-types A and B (69.83%; 97.5% CI: 42.18, 85.72 and 58.57%; 97.5% CI: 35.90, 74.11, respectively), given the lower bound of the 97.5% CI exceeded 0%.

6.26 The resubmission presented exploratory analyses (Table 7) of VE by individual season (as opposed to cumulative seasons shown in Table 5 and Table 6).

Table 7: Individual season-specific VE in participants ≥60 YOA in NH (single dose, mES population, Poisson method, and with season as a covariate)

Endpoint	RSVPreF3 OA				Placebo				VE % % CI [a]
	N[d]	n	T (year)	n/T (per 1000)	N	n	T (year)	n/T (per 1000)	
VE against first occurrence of RSV-LRTD									
End of Season 1 [e]	12,468	7	6,853.2	1	12,498	36	6,837.1	5.3	**80.6 (55.9, 92.7)[b]**
End of Season 2 [e]	4,988	19	2,802.1	6.8	10,031	98	5,609	17.5	**61.4 (36.4, 77.7)[b]**
End of Season 3 [e]	4,988	16	2,552.9	6.3	10,031	60	5,081.3	11.8	**47.2 (7.1, 71.6)**
VE against first occurrence of RT-PCR-confirmed severe RSV-LRTD									
End of Season 1 [f]	12,466	1	6,867.9	0.1	12,494	17	6,867.7	2.5	**94 (62.4, 99.9)[b]**
End of season 2 [f]	4,988	7	4,705.6	1.5	10,031	34	9,462.2	3.6	**58.9 (5.8, 84.6)**
End of Season 3 [f]	4,988	6	2,720.1	2.2	10,031	21	5,421.6	3.9	43.3 (-45.3, 81.3)
VE against first occurrence of RT-PCR-confirmed RSV-ARI									
End of Season 1 [e]	12,468	31	6,845.5	4.5	12,498	90	6,816.8	13.2	**65.7 (48.0, 78.0)[b]**
End of Season 2 [e]	4,988	55	2,788.6	19.7	10,031	204	9,345.8	21.8	**41.9 (21.1, 57.8)[b]**
End of Season 3 [e]	4,988	30	2,548.3	11.8	10,031	111	5,0.65.8	21.9	**46.4 (20.7, 66.1)[b]**

Source: Table 2-26, p100 of the resubmission. Table 18, pp32-34 of the ATAGI advice March 2025.
CI = confidence interval; FUP = follow-up; LRTD = lower respiratory tract disease; mES = modified exposure set; N = number of participants; n = number of participants with at least one RT-PCR-confirmed RSV LRTD/ARI; NH = northern hemisphere; n/T (per 1000) = incidence rate of participants reporting at least one event; RT-PCR = reverse transcription-polymerase chain reaction; RSV = respiratory syncytial virus; RSVPreF3 OA= RSV pre-fusion protein 3 older adult; SH = southern hemisphere; T (year) = sum of follow-up time (from Day 15 post-Dose 1 till first occurrence of the event or till the efficacy data lock point or till drop-out date) expressed in years; VE = vaccine efficacy (Poisson method - adjusted by age, region and season); YOA = years of age.
[a] 95% CI.
[b] Denotes lower limit for 95% CI > 20%.
[d] The number of participants is reduced from end of Season 1 to end of Season 2 and 3 due to participants being censored if they received an additional RSVPreF3 OA dose.
[e] Season 1: 1 October 2021 – 30 April 2022 in NH; 1 March 2022 – 30 September 2022 in SH; median FUP = 6.7 months.
Season 2: 1 October 2022 – 30 April 2023 in NH; 1 March 2023 – 30 September 2023 in SH; cumulative median FUP = 17.8 months for end of season NH; 23.3 months for end of season NH/SH.
Season 3: 1 October 2023 – 30 April 2024 in NH; 1 March 2024 – 30 September 2024 in SH; cumulative median FUP = 30.6 months.
[f] The results for severe RSV-LRTD were sourced from the ATAGI advice March 2025. The PSCR stated 'the ATAGI advice inconsistently reported results for severe RSV-LRTD and RSV-ARI using different season definitions'.
Blue shading indicates results previously seen by the PBAC.
Bold indicates statistically significant results.

6.27 The estimates for VE against RSV in each individual season (Table 7) show lower VE at the end of each season compared to the cumulative results across seasons (Table 6). In Season 3, the lower bound of the 95% CI does not exceed 20%, the criteria for success, for RSV-LRTD (VE = 47.2; 95% CI 7.1, 71.6) and severe RSV-LRTD (VE = 43.3; 95% CI -45.3, 81.3). A lower bound CI <20% was also reported for the first occurrence of severe-RSV LRTD in Season 2 (VE = 58.9; 95% CI 5.8, 84.6).

6.28 The analyses of cumulative VE of a single dose of RSVPreF3 OA against first occurrence of confirmed RSV-LRTD over 3 complete RSV seasons, stratified by age, is presented in Table 8. The resubmission presented a pre-specified subgroup analysis in patients aged 70-79 as a proxy for adults aged ≥75 YOA, and a subgroup analysis for participants ≥80 years, noting the small number of events occurring in this subgroup. The resubmission stated that too few cases of RSV-LRTD accrued in adults of age ≥80 years and frail adults to reliably estimate VE (only 5 cases reported), thus resulting in no difference in VE for that subgroup. The evaluation considered that this was reasonable. Over a period of 3 cumulative RSV seasons, VE was demonstrated for all

age groups except for ≥80 YOA due to low numbers of participants (n=1,017 equivalent to 8.1%) and cases (n=5).

Table 8: Cumulative VE against first occurrence of RSV-LRTD in subgroups of adults based on age, over 3 complete RSV seasons (single dose, mES population and with season as a covariate)

Endpoint	RSVPreF3 OA				Placebo				VE % (CI) [a]; p-value
	N	n	T (year)	n/T (per 1000)	N	n	T (year)	n/T (per 1000)	
Descriptive secondary endpoints (cumulative VE over Season 1 and over Season 1 & 2)									
RSV-LRTD by age group									
Overall trial population (≥60 YOA) – 6.7 m FUP	12,466	7	6,865.9	1.0	12,494	40	6,857.3	5.8	**82.58 (57.89, 94.08); <0.0001**
≥75 YOA[b] – 6.7 m FUP	2,671	3	1,473.5	2.0	2,646	6	1,451.1	4.1	52.48 (-122.52, 92.31); 0.4591
Overall trial population (≥60 YOA) – 17.8 m FUP	12,469	30	14,662.6	2.0	12,498	139	17,269.0	8.0	**67.18 (48.19, 80.04); <0.0001**
≥75 YOA[b] – 17.8 m FUP	2,672	8	3,079.0	2.6	2,647	24	3,624.6	6.6	49.33 (-18.24, 80.56); 0.1312
70-79 YOA	4,489	9	NR	NR	4,489	55	NR	NR	**74.89 (48.42, 89.15)**
Descriptive secondary endpoints (cumulative VE over 3 RSV seasons; median FUP 30.6 months)									
RSV-LRTD by age group									
Overall trial population (≥ 60 YOA)	12,468	48	19,748.8	2.4	12,498	215	27,363.6	7.9	**62.91 (46.74, 74.79); <0.0001**
≥70 YOA	5,506	20	8,608.7	2.3	5,517	98	12,019.8	8.2	**66.0 (44.3, 80.2); <0.0001**
70-79 YOA	4,489	15	7,095.5	2.1	4,489	85	9,866.4	8.6	**70.6 (48.4, 84.3); <0.0001**
≥80 YOA[c]	1,017	5	1,513.2	3.3	1,028	13	2,153.4	6.0	36.2 (-94.0, 82.5); 0.5563

Source: Table 2-22, p94-95 of the resubmission.

CI = confidence interval; FUP = follow-up; LRTD = lower respiratory tract disease; mES = modified exposure set; N = number of participants; n = number of participants with at least one RT-PCR-confirmed RSV LRTD/ARI; RSV = respiratory syncytial virus; RSVPreF3 OA= RSV pre-fusion protein 3 older adult; T (year) = sum of follow-up time (from Day 15 post-Dose 1 till first occurrence of the event or till the efficacy data lock point or till drop-out date) expressed in years; n/T (per 1000) = incidence rate of participants reporting at least one event; VE = vaccine efficacy; YOA = years of age.

Notes:

For single dose evaluation, participants who received RSVPreF3 OA at Dose 2 (RSV_annual group) were censored at Dose 2.

VE (%) = vaccine efficacy (Poisson method - adjusted by age, region and season); *VE (%) = Vaccine Efficacy (Poisson method - adjusted by region and season).

P-value = Two sided exact p-value conditional on number of cases comparing incidence rates and testing the null hypothesis VE ≤ 0%.

Follow-up as per footnotes to Table 7.

[a] 96.95% CI for primary endpoint (RSV-LRTD, season 1); 97.5% CI for confirmatory secondary endpoint (RSV-LRTD, season 1 + 2 + 3); 95% CI for other endpoints (including post-hoc analysis).

[b] Post-hoc subgroup analysis presented in the July 2024 submission.

[c] There were insufficient RSV-LRTD cases in adults ≥80 YOA to reliably conclude efficacy.

Blue shading indicates results previously seen by the PBAC.

Bold text indicates statistically significant result.

6.29 No statistically significant differences between the RSVPreF3 OA group and placebo group were observed in terms of physical functioning (SF-12) nor health related quality of life (EQ-5D) in participants who developed RSV-ARI (data not shown). However, statistically significant differences were observed in the FLU-PRO chest/respiratory item, indicating that participants in the RSVPreF3 OA arm had fewer symptoms such as trouble breathing, chest tightness and frequency and severity of

cough, compared to participants in the placebo group. This effect decreased over time; the end of Season 3 results show that the difference in mean score for FLU-PRO was reduced from 0.58 at the end of Season 1 to 0.37 at the end of Season 3. Prior analyses of the FLU-PRO in patients with and without influenza have shown that changes in the item scores of <0.5 are not clinically meaningful[3].

6.30 Supportive evidence from RSV OA=ADJ-004 indicated that the neutralising titres for RSV A and B, measured as mean geometric titres (GMT), increase following Dose 1 and then decrease at 6 months (data not shown). Beyond 6 months, the titres continue to decrease, albeit less markedly by 12 months post vaccination. The resubmission stated that between Month 24 and Month 36, the titres in the RSVPreF3 OA group stabilised at a plateau above the pre-vaccination levels.

Indirect treatment comparison – RSVPreF3 OA (Arexvy) vs RSVPreF (Abrysvo)

6.31 The results of the unadjusted unanchored ITC are presented in Table 9. The resubmission stated that this type of ITC was appropriate due to the high degree of heterogeneity between the trials with insufficient exchangeability of the trial designs, populations, outcome measures, statistical analyses, definition of RSV seasons and follow-up periods.

[3] Yu J, Powers JH 3rd, Vallo D, Falloon J. Evaluation of Efficacy Endpoints for a Phase IIb Study of a Respiratory Syncytial Virus Vaccine in Older Adults Using Patient-Reported Outcomes With Laboratory Confirmation. Value Health. 2020 Feb;23(2):227-235. doi: 10.1016/j.jval.2019.09.2747. Epub 2019 Nov 21. PMID: 32113628.

Table 9: Unadjusted unanchored indirect comparison of cumulative VE of RSVPreF3 OA and the RSVpreF vaccine over consecutive RSV seasons, including in adults aged 70-79 YOA

VE% (CI)	Cohort	RSVPreF3 OA (AReSVi-006) N= 25,040				RSVpreF (RENOIR) N= 34,284			
		Median VE FUP	RSV-LRTD ≥2 or ≥3 symptoms/signs		RSV-ARI	Mean VE FUP	RSV-LRTI≥2 symptoms	RSV-LRTI≥3 symptoms	RSV-ARI
			With season as covariate (protocol)	Without season as covariate (post hoc)	With season as covariate (protocol)		Without season as covariate		
Primary analysis Over Season 1 (case-driven)	≥ 60 YOA	6.7 m (NH)	82.6 96.95% CI: 57.9, 94.1	NA	71.7 95% CI: 56.2, 82.3	7.0 m (NH/SH)	66.7 96.66% CI: 28.8, 85.8	85.7 96.66% CI: 32, 98.7	62.2 95% CI: 44.4, 74.9
	70-79 YOA		93.8 95% CI: 60.2, 99.9	NA	87.6 95% CI: 65.1, 96.8		77.8 96.66% CI: -18.7, 98.1	100 96.66% CI: -573.8, 100	64.3 95% CI: -4.9, 89.9
Over Season 1 & 2 VE	≥ 60 YOA	17.8 m (NH)	67.2 97.5% CI: 48.2, 80.0	74.5 97.5% CI: 60.0, 84.5	52.7 95% CI: 40.0, 63.0	16.4 m (NH/SH)	58.8 95% CI: 43.0, 70.6	81.5 95% CI: 63.3, 91.6	44.3 95% CI: 33.2, 53.7
	70-79 YOA		74.9 95% CI: 48.4, 89.2	80.7 95% CI: 60.6, 91.6	NR		62.5 95% CI: 30.6, 80.8	72.7 95% CI: -3.2, 95.1	43.8 95% CI: 19.7, 61.1
	≥ 60 YOA	23.3 m (NH/SH)	67.7 95% CI: 52.3, 78.7	73.3 95% CI: 60.7, 82.4	52.0 95% CI: 39.5, 62.1	Data not reported over similar duration of follow-up			
Over Season 1, 2 & 3 VE	≥ 60 YOA	30.6 m (NH)	62.9 97.5% CI: 46.7, 74.8	69.1 97.5% CI: 46.7, 74.8	51.1 95% CI: 40.3, 60.2	No protocol-specified follow-up of VE beyond 24 months			
	70-79 YOA		70.6 95% CI: 48.4, 84.3	75.6 95% CI: 57.5, 86.9	62.3 95% CI: 45.6, 74.4				

Source: Table 2-36, p144 of the resubmission.

ARI = acute respiratory infection; CI = confidence interval; FUP = follow up; LRTD/LRTI = lower respiratory tract disease/infection; m = months; NA = not applicable; NH = Northern Hemisphere; NR = not reported; S = season; S= Southern Hemisphere; RSVPreF = recombinant RSV prefusion F protein vaccine; RSVPreF3 OA = RSV pre-fusion protein 3 older adult; VE = vaccine efficacy; YOA = years of age.

Blue shading reflect data previously seen by the PBAC.

Note that the results for the naïve indirect treatment comparison presented, including the post-hoc analysis of RSVPreF3 OA VE without season as a covariate, are derived from ad-hoc/post-hoc analyses specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for RSV OA=ADJ-006 or RENOIR. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.

6.32 The following can be drawn from the results presented in Table 10[4]:

- The resubmission stated that RSVPreF3 OA and RSVpreF vaccines appear to have similar VE against RSV-LRTD in adults ≥60 YOA for the primary analysis (Season 1) and for RSV Season 2 after similar periods of follow-up (approximately 18

[4] Note that the results for the naïve indirect treatment comparison presented, including the post-hoc analysis of RSVPreF3 OA VE without season as a covariate, are derived from ad-hoc/ post-hoc analyses specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for RSV OA=ADJ-006 or RENOIR. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.

months). ATAGI concurred stating that, noting limitations in the naïve ITC presented, VE against RSV-LRTD was similar for RSVPreF3 OA compared with RSVpreF (ATAGI advice, March 2025).

- The resubmission stated that RSVPreF3 OA has demonstrated durable clinically meaningful VE against RSV-LRTD in adults ≥60 YOA over a median 30.6 months of follow-up (VE = 69%, without season as covariate). Data are not publicly reported for RSVpreF beyond a mean of 16 months of follow-up, therefore, an indirect comparison of VE could not be made for RSVPreF3 OA compared with RSVpreF beyond the first 16 months after vaccination. The evaluation noted that the absence of longer-term VE data does not mean RSVPreF is not effective beyond 16 months.
- The ATAGI stated that numerically, VE against RSV-LRTD is higher with RSVPreF3 OA compared with RSVpreF in adults aged 70-79 YOA (ATAGI advice, March 2025). However, the evaluation noted that these comparisons should be interpreted with caution given they are based on subgroup analyses with small sample sizes, a limited number of cases, and are subject to differences between trials (in endpoint definitions and durations). The evaluation considered that the evidence presented does not support superior efficacy of RSVPreF3 OA against RSVPreF for adults aged 70-79, given that the ITCs were unanchored and unadjusted and by definition were not powered for claims of superiority.
- The resubmission stated that due to the different case definitions of ARI between the trials, conclusions on the comparative VE of RSVPreF3 OA and RSVpreF could not be made. The evaluation considered that this was not reasonable. While the RSV-ARI definition used in the AReSVi-006 trial appears more stringent than that in the RSVpreF RENOIR trial, potentially leading to fewer cases being classified as disease, this would impact the comparison of absolute case numbers across trials but not the relative difference between the vaccine and placebo arms within the trials. Notwithstanding, the evaluation considered that while there is an apparent numerical difference in VE in favour of RSVPreF3 OA, the CIs overlap and the difference could be due to random variation.
- Due to differences in the case definition of severe RSV across the trials, the resubmission did not present an ITC for this outcome. ATAGI stated that these differences would not preclude conduct of a naïve ITC (ATAGI advice, March 2025).

Comparative harms

RSVPreF3 OA (Arexvy) versus placebo

6.33 A summary of the solicited adverse events (AEs) comprising any AE, administration site AE, systemic AE, and Grade 3 AEs is presented in Table 10. These results remain unchanged from the July 2024 submission.

Table 10: Summary of solicited adverse events, any Grade and Grade 3, within 4-days following each dose and overall (SSS)

Trial ID	RSVPreF3 OA (overall) n with event/N (%)	Placebo n with event/N (%)
Any grade		
Any AE	632/879 (71.9)	245/878 (27.9)
Admin-site AE	548/879 (62.3)	87/878 (9.9)
Systemic AE	435/879 (49.5)	204/878 (23.2)
Grade 3		
Any AE	36/879 (4.1)	8/878 (0.9)
Admin-site AE	13 [a]	13 [a]
Systemic AE	29/879 (3.3)	8/878 (0.9)

Source: Table 2-27 and Table 2-28, p102-103 of the resubmission.
AE = adverse event; N = number of participants with a diary card; RSVPreF3 OA= RSV prefusion F protein older adult vaccine (RSV_annual + RSV_1dose); SSS = solicited safety set
[a] Due to the small number of events, events are represented across all study arms in order to maintain blinding.
RSVPreF3 OA includes the single dose and the first vaccination of the revaccination arm
Bue shading shows results previously seen by the PBAC.

6.34 A summary of unsolicited AEs occurring within 30 days following vaccination was reported in the exposed set (Table 11). The majority (93%) of participants in the RSVPreF3 OA exposed set (who were not included in the solicited safety set, SSS) recorded all AEs experienced within 30 days as unsolicited AEs, including reactogenicity events.

Table 11: Summary of unsolicited AEs following vaccination, exposed set

	RSVPreF3 OA (overall) n with event/N (%)	Placebo n with event/N (%)	RR[a] (95% CI)
Unsolicited AEs within 30 days post-vaccination			
Any grade AE	4,285/12,469 (34.4)	2,334/12,503 (18.6)	1.84 (1.75, 1.94)
Any Grade 3 AE	251/12,469 (2.0)	158/12,503 (1.3)	1.59 (1.30. 1.96)
Any AE related to the intervention	3,226/12,469 (25.9)	760/12,503 (6.1)	NR
Any Grade 3 related to the intervention	110/12,469 (0.9)	23/12,503 (0.2)	NR
Atrial fibrillation[b]	11/12,469 (0.1)	4/12,503 (0.0)	2.76 (0.82,11.87)
Unsolicited AEs up to 6 months post-vaccination			
Any SAE D1	548/12,469 (4.4)	541/12,503 (4.3)	1.02 (0.94, 1.10)
Any pIMD D1	46/12,469 (0.4)	39/12,503 (0.3)	1.18 (0.87, 1.60)
Any pIMD related to the intervention	8/12,469 (0.1)	7/12,503 (0.1)	
Unsolicited events post each dose up to end of Season 3			
Any fatal SAE	231/12,469 (1.9)	265/12,503 (2.1)	NR
SAE of atrial fibrillation within 6 months post vaccination			
D1	15/12,469 (0.1)	16/12,503 (0.1)	0.94 (0.56, 1.59)
D2	11/4,968 (0.2)	13/10,033 (0.1)	1.71 (0.93, 3.13)
D3	4/1,409 (0.3)	16/2,866 (0.6)	0.51 (0.2, 1.15)

Source: Compiled during the evaluation from information provided in the resubmission, pp106-110. End of Study CSR, pp441-442; pp448-449, p495, p583, pp48-53, pp3764-3765 and p9357.
AE = adverse event; CI = confidence interval; CSR = clinical study report; D = dose; n = number of participants reporting data in at least one event; N = total participants in group; pIMD = potential immune-mediated disorders; NR = not reported; RSVPreF3 OA= RSV pre-fusion protein 3 older adult; RR = relative risk; SAE = serious adverse events.
[a] RR only included if reported in the resubmission or CSR.
[b] Includes serious and non-serious AEs.
Blue shading reflect data previously seen by the PBAC

6.35 Atrial fibrillation (AF) was a specific AE of interest, with more cases among RSVPreF3 OA versus placebo (11 and 4 cases, respectively) post vaccination. Most AF events

were mild or moderate (7 of the 11), none resulted in withdrawal, and almost all resolved (10 of the 11 in the RSVPreF3 OA arm and 3 of 4 in the placebo arm). SAEs within 6 months were balanced between the arms and the incidence was low.

Indirect treatment comparison – RSVPreF3 OA (Arexvy) vs RSVPreF (Abrysvo)

6.36 The resubmission stated that the results of the unanchored unadjusted ITC of solicited AEs and unsolicited AEs for RSVPreF3 OA and RSVPreF showed a similar overall safety profile. The resubmission noted that collection of unsolicited AEs in the overall safety population differed for AReSVi-006 (all AEs including reactogenicity events were recorded as unsolicited in 93% of the cohort not included in the SSS) versus RENOIR (approximately 80% not in the SSS), resulting in higher rates of unsolicited AEs in AReSVi-006, the majority of which were reactogenicity events (comparative data not shown). Rates of solicited and unsolicited AEs were broadly similar in the common reference placebo arms of AReSVi-006 and RENOIR.

6.37 The safety results from RSV OA=ADJ-004 were comparable to those reported in AReSVi-006 for any AEs. However, a higher proportion of participants experienced a Grade 3 AE in RSV OA=ADJ-004 (11%) compared to AReSVi-006 (4.1%). In the July 2024 PBAC consideration, it was noted that data from RSV OA=ADJ-004 showed reactogenicity and safety profiles for revaccination at 12 and 24 months were similar to those at the first dose (paragraph 6.22, RSVPreF3 OA PSD, July 2024).

Benefits/harms

RSVPreF3 OA (Arexvy) versus placebo

6.38 A summary of the comparative benefits and harms for RSVPreF3 OA versus placebo is presented in Table 12.

Table 12: Summary of comparative benefits and harms for RSVPreF3 OA and placebo

Benefits				
RT-PCR confirmed RSV-LRTD				
Event	**RSVPreF3 OA**	**Placebo**	**Absolute Difference**	
≥60 YOA over cumulative seasons				**Cumulative VE% (CI [a])**
Over Season 1	7/12,466 (0.1%)	40/12,494 (0.3%)	33 (0.3%)	**82.6 (57.9, 94.1)**
Over Season 1 & 2	30/12,469 (0.2%)	139/12,498 (1.1%)	109 (0.9%)	**67.2 (48.2, 80.0)**
Over Season 1, 2 & 3	48/12,468 (0.4%)	215/12,498 (1.7%)	167 (1.3%)	**62.9 (46.7, 74.8)**
≥60 YOA by individual season				**VE% by season (CI [a])**
End of Season 1	7/12,466 (0.1%)	36/12,498 (0.3%)	29 (0.2%)	**80.6 (55.9, 92.7)**
End of Season 2	19/4,988 (0.4%)	98/10,031 (1.0%)	79 (0.6%)	**61.4 (36.4, 77.7)**
End of Season 3	16/4,988 (0.3%)	60/10,031 (0.6%)	44 (0.3%)	**47.2 (7.1, 71.6)**

Harms ≥60 YOA						
AReSVi-006	**RSVPreF3 OA n/N**	**Placebo n/N**	**RR (95% CI)**	**Event rate/100 patients**		**RD (95% CI)**
				RSVPreF3 OA	**Comparator/ Placebo**	
Solicited Grade 3 events within 4 days following dose 1						
Any AE	36/879	8/878	4.49 (2.10, 9.62)	4.10	0.91	0.032 (0.02, 0.05)
Admin-site AE	13 [b]	13 [b]	NA	NA	NA	NA
Systemic AE	29/879	8/878	3.62 (1.67, 7.88)	3.30	0.91	0.024 (0.01, 0.04)
Unsolicited AEs within 30 days post vaccination						
Any Grade 3	251/12,469	158/12,503	1.59 (1.31, 1.94)	2.01	1.26	0.007 (0.00, 0.01)
Any Grade 3 related to the intervention	110/12,469	23/12,503	4.79 (3.06, 7.51)	0.88	0.18	0.007 (0.005, 0.009)
Any medically attended	718/12,469	722/12,503	1.00 (0.90, 1.10)	5.76	5.77	0.000 (-0.01, 0.01)
Unsolicited AEs within 6 months post vaccination						
Any SAE	548/12,469	539/12,503	1.02 (0.91, 1.15)	4.39	4.31	0.001 (-0.00, 0.01)
Any SAE related to the intervention	15/12,469	10/12,503	1.50 (0.68, 3.35)	0.12	0.08	0.001 (0.00,0.00)
Any pIMD	46/12,469	38/12,503	1.21 (0.79, 1.86)	0.37	0.30	0.001 (-0.00, 0.00)
Any pIMD related to the intervention	8/12,469	7/12,503	1.15 (0.42, 3.16)	0.03	0.06	0.000 (-0.00, 0.00)
Any fatal SAE	231/12,469	265/12,503	0.87 (0.73, 1.04)	1.85	2.12	-0.003 (-0.00, 0.00)

Source: Table 2-19, p100; Table 22-20, p115; Table 2-21, p103; Table 2-31, pp118-119 of the submission. Compiled during the evaluation from evaluation from Table 12.4, p296 of 'RSV OA = Adj-006 Study Report (Blinded End of Season 2) 28 Jun 2023' of the Submission.
admin = administration; AE = adverse event; CI = confidence interval; ES = exposed set; mES = modified exposed set; N = number of participants; n = number of participants with at least one RT-PCR confirmed RSV-LRTD; LRTD = lower respiratory tract disease; n/T (per 1000) = incidence rate of participants reporting at least one event; RD = risk difference; RR = relative risk; RSV = respiratory syncytial virus; RSVPreF3 OA= RSV pre-fusion protein 3 older adult; RT-PCR = reverse transcription-polymerase chain reaction; T (year) = sum of follow-up time (from Day 15 post-vaccination till first occurrence of the event or till the efficacy data lock point or till drop-out date) expressed in years; VE = vaccine efficacy.
Note:
[a] ≥ 60: VE analysis 1 = 96.95% CI; VE analysis 2 = 95% CI and VE analysis 3 = 97.5% CI. ≥ 60: VE analysis 1, 2 and 3 = 95% CI.
[b] Due to the small number of events, events are represented across all study arms in order to maintain blinding.
VE analysis 1: median duration of follow up = 6.7 months. VE analysis 1: median duration of follow up = 11.5 months. VE analysis 3: median duration of follow up = 17.8 months
Blue shading reflects data previously seen by the PBAC.
RR and RD calculated for the evaluation and should be considered as indicative as the study was not powered for comparisons of safety.
Bold indicates statistically significant results.

6.39 On the basis of direct evidence presented by the submission, for every 1,000 individuals ≥60 YOA vaccinated with a single dose of RSVPreF3 OA, in comparison with placebo (no vaccine):

- Approximately 13 fewer adults will have RT-PCR confirmed RSV-LRTD over 3 cumulative RSV infection seasons.
- Between 2 to 6 fewer adults will have RT-PCR confirmed RSV-LRTD per individual RSV infection season (over the first three seasons since vaccination).
- Approximately 32 additional adults would experience any Grade 3 solicited events within 4 days of vaccination.
- Approximately 24 additional adults would experience grade 3 systemic solicited events within 4 days of vaccination.
- Approximately 7 additional adults would experience any Grade 3 unsolicited AEs within 30 days of vaccination.
- Approximately 7 additional adults would experience any Grade 3 unsolicited AEs related to RSVPreF3 OA within 30 days of vaccination.

Clinical claim

RSVPreF3 OA (Arexvy) versus placebo

6.40 The submission described RSVPreF3 OA as superior in terms of VE compared with no vaccine. The ESC and PBAC agreed with the evaluation that this claim was adequately supported, however, some issues were noted as follows:

- The cumulative estimate of VE over 3 seasons (62.9%) was lower than those reported at the end of Season 1 (82.6%) and Seasons 1 and 2 (67.2%) in the AReSVi-006 trial (Table 5). This pattern of VE reflects the waning over time of a single dose RSVPreF3 OA (over a median follow-up of 6.7 months to 30.6 months). VE beyond Season 3, optimal timing for revaccination, and VE associated with revaccination have not yet been determined and remain unknown. The PSCR indicated that future follow-up from the pivotal immunogenicity trial, RSV OA=ADJ-004, and an immunogenicity extension and crossover of AReSVi-006 (RSV OA=ADJ-012) will assess the immune persistence of a single vaccine dose and alternate revaccination schedules up to Month 60 after initial vaccination. The ESC noted these studies are ongoing and were designed to also include alternate revaccination schedules at 24- or 36-month intervals (AReSVi-004) and before Seasons 4 or 5 (RSV OA=ADJ-012). Thus, the ESC reiterated that the optimal timing for revaccination is unknown but revaccination at 3 and 4 years is being assessed in the clinical studies (refer paragraph 6.59).
- For the Season 3 individual season results, the lower bound of the 95% CI did not exceed the pre-defined threshold of 20% for first occurrence of RSV-LRTD

(VE = 47.2; 95% CI 7.1, 71.6) and severe RSV-LRTD (VE = 43.3; 95% CI -45.3, 81.3). Comparison of season specific effects was an exploratory analysis within the AReSVi-006 trial.

- No data were presented to support the requested listing for Aboriginal and Torres Strait Islander people. However, VE as demonstrated in the AReSVi-006 trial is anticipated to be applicable to this high-risk group. Additionally, it is unlikely that direct evidence in this population will ever become available. Thus, the evaluation considered that extension of the clinical claim to Aboriginal and Torres Strait Islander people may be reasonable.

6.41 The pre-PBAC response provided [redacted].

6.42 The submission described RSVPreF3 OA as having an acceptable safety profile despite being more reactogenic compared to placebo. The ESC and the PBAC agreed with the evaluation that this claim was adequately supported by the available evidence.

Indirect treatment comparison – RSVPreF3 OA (Arexvy) versus RSVPreF (Abrysvo)

6.43 The resubmission stated that RSVPreF3 OA was the only vaccine that has demonstrated durable and clinically meaningful efficacy over 3 complete RSV seasons, while RSVPreF has been shown to be effective for 2 RSV seasons. The evaluation considered that the lack of end-of-Season 3 data for RSVpreF should not be interpreted as indicative of inferior performance compared to RSVPreF3 OA; it reflects an absence of evidence, not evidence of RSVpreF 3 OA being superior.

6.44 The evaluation noted that according to ATAGI, results for the naïve (i.e., unadjusted unanchored) ITC are likely more supportive for a claim of non-inferiority, noting that the evidence presented for the duration of protection for the vaccines was limited by the duration of follow up reported by each trial (ATAGI advice, March 2025).

6.45 The PSCR disagreed with this approach, stating that based on the duration of follow-up from the respective trials, RSVPreF has demonstrated efficacy over 2 RSV seasons and RSVPreF3 OA has demonstrated efficacy over 3 RSV seasons. The PSCR considered that application of a cost minimisation approach based on presumed non-inferiority of RSVPreF3 OA to RSVpreF would be inconsistent with the available clinical evidence. The PSCR argued that the cost-effectiveness of each RSV vaccine would be best informed by their respective CUA.

6.46 The ESC acknowledged the limitations of the indirect comparison (e.g. it was unadjusted and unanchored, and there were differences in outcome definitions between trials) but concluded that, over the time period for which there is data available for both vaccines (approximately 18 months), it is likely that RSVPreF3 OA is non-inferior to RSVPreF.

6.47 The PBAC agreed with the ESC that over the time period for which there is data available for both vaccines (2 seasons), it was likely that RSVPreF3 OA is non-inferior to RSVPreF. The PBAC further considered that non-inferiority could be extended to

the third season on the basis that the lack of data for RSVpreF for season 3 was not interpreted as indicative of inferior performance compared to RSVPreF3 OA, rather it reflected an absence of clinical evidence to date. The PBAC considered that based on the data available for clinical and immunological endpoints, it was plausible that the similar performance observed across the first two seasons would extend to year three.

6.48 The PBAC also noted that while evidence was available for RSVPreF3 OA, the point estimates for the season-specific results for RSVPreF3 OA revealed notably lower VE in Season 3 than was evident from the cumulative VE estimates, and there were wide confidence intervals for the season-specific results in Season 3. Notably, the lower bound of the 95% CI did not exceed 20%, the nominated criteria for success, for RSV-LRTD (VE =47.2; 95% CI 7.1, 71.6) and severe RSV-LRTD (VE = 43.3; 95% CI -45.3, 81.3).

6.49 The PBAC noted the limitations of the indirect comparison presented in the resubmission, including the different durations of trial follow-up available, and on balance concluded that RSVPreF3 OA was non-inferior to RSVPreF with respect to comparative effectiveness and comparative safety.

Economic analysis

6.50 The resubmission presented an economic evaluation comparing a single dose of RSVPreF3 OA with no vaccine based on data from AReSVi-006 and implementing a modelled evaluation (CUA) for adults ≥75 YOA and Aboriginal and Torres Strait Islander people 60-74 YOA.

6.51 At its July 2024 meeting, the PBAC noted that if revaccination is requested in the future, this would influence cost-effectiveness (paragraph 6.88 and 7.21, RSVPreF3 OA PSD, July 2024). The resubmission did not present a cost-effectiveness analysis which included revaccination, stating that the need and optimal timing of revaccination is not yet established.

6.52 A summary of the model structure, key inputs and rationale is presented in Table 13. The model is largely similar to that presented in the July 2024 submission. Key inputs updated in the resubmission include:

- VE and waning data.
- RSV-associated hospitalisation rates, including updated under-ascertainment multipliers and unadjusted RSV hospitalisation rates.
- RSV-associated hospitalisation costs.
- RSV-related death.

Table 13: Summary of model structure, key inputs and rationale

Component	July 2024 submission	July 2025 resubmission[a]
Populations	• ≥ 60 YOA • ≥ 75 YOA • ≥ 65 YOA, ≥ 70 YOA, and ≥ 80 YOA	• ≥ 75 YOA • Aboriginal and Torres Strait Islander people 60-74 YOA
Treatments	RSVPreF3 OA versus no vaccine	Unchanged
Outcomes	LYs and QALYs	Unchanged

Component	July 2024 submission	July 2025 resubmission[a]
Time horizon	3-year duration of protection, lifetime for LYs and QALYs	5-year duration of protection, lifetime for LYs and QALYs
Methods used to generate results	Static multi-cohort Markov model	Unchanged
Health states	No-RSV, post-RSV (participants that survived at least one RSV episode), and death	Unchanged
Cycle length	1 month	Unchanged
Transition probabilities		
Vaccine efficacy	Linear model. Per AReSVi-006 (overall population): 18 months Waning: 25 months for RSV-LRTD, 16 months for RSV-ARI. A PSCR-revised analysis based on a median follow-up of 23.3 months.	Linear logarithmic model. Per AReSVi-006 (overall population): 3 years (median 30.6-month trial data). Waning: 2 years (assuming constant decline rate).
Vaccination month	March	All months, using an annual average
RSV-associated hospitalisation rates: Under-ascertainment multipliers	2.19 (Li et al. 2023)	≥75 YOA: a multiplier of 2.0 (under-testing correction; ATAGI) and 1.5 (under-ascertainment multiplier for test sensitivity based on 66% sensitivity of RT-PCR of nasopharyngeal swabs; Havers et al., 2024a; Mclaughlin et al., 2022; Onwuchekwa et al., 2023). PSCR: used a 2.0 multiplier only, but applied this to AIHW data from 2018–2019. Aboriginal and Torres Strait Islander people 60-74 YOA: equivalent to adjusted RSV-associated hospitalisation rates of the ≥75 YOA population[b]. PSCR: assumed 1.5 times the rate estimated for the ≥ 75 YOA population.
Unadjusted RSV-associated hospitalisation rates	Branche et al. 2022	≥75 YOA: AIHW NHMD 2016-2019. PSCR: ≥75 YOA: AIHW NHMD 2018-2019 only. Aboriginal and Torres Strait Islander people 60-74 YOA: AIHW NHMD 2016-2019. PSCR: assumed 1.5 times the rate estimated for the ≥75 YOA population.
Annual RSV incidence	Unadjusted: 2.61/100 person-years (Korsten et al. 2021; Narejos Pérez et al. 2023). Adjusted: 5.72/100 person-years (2.61 x 2.19 from Li et al. 2023)	Unadjusted: unchanged Adjusted: 3.95/100 person-years (2.61 x 1.5 from Havers et al., 2024a; Mclaughlin et al., 2022; Onwuchekwa et al., 2023)
RSV-related deaths	Tseng et al. 2020	2012-2019 AIHW NHMD PSCR: changed to a 4.22% RSV-hospital case fatality rate, based on ATAGI advice 2025, consistent with para 7.17, Abrysvo PSD, Nov 2024.
Background mortality	ABS lifetables	≥75 YOA population: unchanged Aboriginal and Torres Strait Islander people 60-74 YOA: Aboriginal and Torres Strait Islander people ABS lifetables
Adverse events	Grade 3 (severe) AE: 2.27% (Grade 3 AE from AreSVi-006 vaccinated arm)	Unchanged

Component	July 2024 submission	July 2025 resubmission[a]
HRQoL	Population norms: McCaffrey et al. 2016. (0.89 for 60-64 YOA, 0.87 for 65-74 YOA, and 0.83 for ≥75 YOA) Vaccine-related AE: Schmader et al. 2019 (per Grade 3 AE estimated at 0.000677). RSV-LRTD and RSV URTD utility decrements: US TTO study (0.025 for severe RSV-LRTD, 0.018 for RSV-LRTD, and 0.013 RSV-URTD)	Population norms: Redwood et al. 2024 (0.86 for 60-64 YOA, 0.88 for 65-74 YOA, and 0.86 for ≥75 YOA) PSCR: unchanged for ≥75 YOA population; baseline utility of 0.675 applied to Aboriginal and Torres Strait Islander people 60-74 YOA population, consistent with Table 11, Abrysvo PSD, Nov 2024. Vaccine-related AE: unchanged RSV-LRTD and RSV URTD utility decrements: unchanged.
Hospitalisation costs	NEP 2023, NHCDC cost weights & separations: 2019-20. LOS *{Ward cost per day*(1-% ICU admitted) + [ICU without MV cost per day *(% ICU admitted-% MV use)]+ (ICU with MV cost per day *MV use)}.	Hitch et al., 2024 ($20,091, Adjusted mean, 2024 values) PSCR: included scenario analyses which tested other hospitalisation costs including Brusco et al 2022 ($16,693) and expert opinion ($15,525 based on AR-DRG E62A-B, inflated by 50%)
Administration cost	Not included	$9.8 per administration (MBS Item 3, 50% co-vaccination assumption) PSCR: $7.00 consistent with Abrysvo PSD, Nov 2024 (based on marginal administration i.e. 36% of MBS Item 3 which has a fee of $19.60)

Source: Complied during the evaluation based on Table 14, RSVPreF3 OA PSD, July 2024; Section 3 of the resubmission.
ABS = Australian Bureau of Statistics; AE = adverse event; AIHW = Australian Institute of Health and Welfare; ARI = acute respiratory infection; ATAGI = Australian Technical Advisory Group on Immunisation; HRQoL = health-related quality of life; ICU = intensive care unit; LOS = length of stay; LRTD = lower respiratory tract disease; LYs = life years; MV = mechanical ventilation; NEP = National Efficient Price; NHCDC = National Hospital Cost Data Collection; NHMD = National Hospital Morbidity Database; MBS = Medicare Benefits Schedule; MV = mechanical ventilation; PBAC = Pharmaceutical Benefits Advisory Committee; PSCR = Pre-subcommittee response; QALYs = quality-adjusted life years; OA = older adults; RSV = respiratory syncytial virus; RT-PCR = reverse transcription polymerase chain reaction; TTO = time trade-off; URTD = upper respiratory tract disease, YOA = years of age.
[a] Unless stated otherwise, the same approach/inputs used for ≥75 YOA and Aboriginal and Torres Strait Islander people 60-70 YOA.
[b] Based on the economic model worksheet "ResubUpdates".

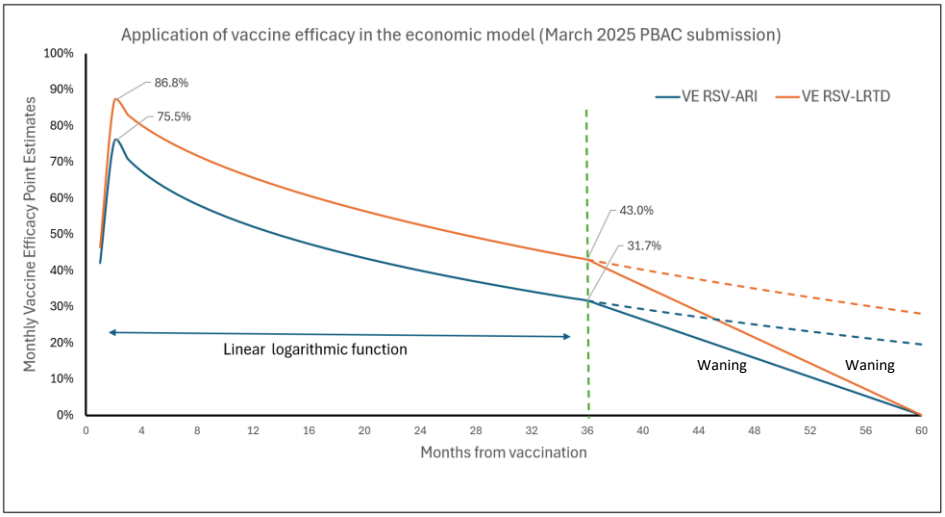
6.53 The resubmission applied the same modelling approaches used for adults ≥75 YOA to the Aboriginal and Torres Strait Islander people 60-74 YOA population, while incorporating specific inputs including RSV-associated hospitalisation rates, RSV-related death, and background natural mortality. The resubmission used the same efficacy from AReSVi-006 (overall population based on adults ≥60 YOA) applied to both the Aboriginal and Torres Strait Islander people 60-74 YOA and ≥75 YOA populations, acknowledging that the efficacy of RSVPreF3 OA in Aboriginal and Torres Strait Islander adults is currently unknown. This approach aligns with the previous submission for RSVPreF (Abrysvo, November 2024), where efficacy estimates from adults aged ≥60 years were applied across different population groups. For the RSVPreF consideration, the PBAC noted the lack of information on differential immune response or safety in Aboriginal and Torres Strait Island people and acknowledged potentially lower VE due to higher rates of medical risk factors and comorbidities in this population. Nevertheless, it was considered appropriate to apply the same VE values across all population groups for RSVPreF (paragraph 6.38 and 6.45, RSVPreF PSD, November 2024).

6.54 In its July 2024 consideration of RSVPreF3 OA, the PBAC noted that the model assumed VE over a 3-year period, but limited data were available to estimate the duration of protection (paragraph 6.88, RSVPreF3 OA PSD, July 2024). In response, as part of its

request for ATAGI advice, the resubmission presented an analysis of VE based on updated data from AReSVi-006 with a median follow-up of 30.6 months for 3 RSV seasons duration of protection (ATAGI Advice, March 2025). The ATAGI accepted RSVPreF3 OA offered prevention from RSV for at least 3 seasons in adults ≥60 YOA, based on secondary confirmatory endpoints (cumulative efficacy), while noting that its efficacy beyond 3 seasons remained unknown (ATAGI Advice, March 2025).

6.55 The outputs from the revised analysis for VE used in the economic model from the resubmission are presented in Figure 1, and a comparison with those data and the clinical data from AReSVi-006 is shown in Table 14.

Figure 1: Application of VE against RSV-LRTD and RSV-ARI in the economic model (July 2025 PBAC resubmission)



ARI = acute respiratory infection, LRTD = lower respiratory tract disease, RSV = respiratory syncytial virus, VE = vaccine efficacy
Source: Figure 3-14, p215 of the July 2025 resubmission.
Note: Dashed lines represent extrapolated vaccine effectiveness estimates (as applied in the resubmission) beyond the trial period, based on a linear logarithmic model.

Table 14: A comparison of trial-based AReSVi-006 and modelled vaccine efficacy

Time point	July 2025 economic model (linear logarithmic model)	July 2024 economic model (linear model)	AreSVi-006	
			Season specific	Cumulative efficacy (season adjusted)
RSV-LRTD				
Peak VE RSV-LRTD (30 days)[a]	86.83%	88.02%	Season 1: 80.6%	NR
7 months	73.55%	75.42%		82.58%
12 months	65.70%	64.92%		78.86%
18 months	58.53%	52.32%	Season 2: 61.4%	67.18%
24 months	52.64%	39.72%		67.7%
30 months	47.55%	27.12%	Season 3: 47.2%	62.9%
36 months	43.00%	14.52%		NA
RSV-ARI				
Peak VE RSV-ARI (30 days)[a]	75.48%	74.17%	Season 1: 65.7%	NR
7 months	60.06%	61.61%		71.71%
12 months	52.09%	49.31%		64.20%
18 months	45.29%	35.75%	Season 2: 41.9%	52.74%
24 months	39.96%	22.19%		NR
30 months	35.51%	8.63%	Season 3: 46.4%	51.1%
36 months	31.65%	0.00%		NA

Source: Table 15, RSVPreF3 OA PSD, July 2024; Table 2-18, p88, Table 2-26, p100 of the July 2025 resubmission; Worksheet 'Efficacy' of the July 2025 resubmission economic model; Worksheet 'Efficacy' of the July 2024 resubmission economic model

ARI = acute respiratory infection; LRTD = lower respiratory tract disease; NA = not applicable; NR = not reported; RSV = respiratory syncytial virus; VE = vaccine efficacy.

[a] Peak VE was modelled between 15 days to 45 days post-vaccination consistent with the timing.

Blue shading indicates data previously seen by the PBAC.

6.56 The resubmission used a linear logarithmic function to inform VE over the first 3 years of the economic model. The ATAGI noted no specific issues with the proposed linear logarithmic function (ATAGI Advice, March 2025). The evaluation considered that the linear logarithmic function likely provided a more accurate representation of the slower decline in VE observed over time from the updated VE data, compared to the linear function used in the July 2024 submission. The VE predicted by the linear logarithmic function is generally comparable to the season-specific efficacy.

6.57 The resubmission assumed 2 years of constant waning (following the first 3 years) until convergence to 0% at 5 years (1.8% per month for LRTD and 1.3% per month for ARI). The ATAGI did not explicitly suggest any preferred waning assumptions but considered that presenting sensitivity analyses where there is truncation of VE at 4 or 5 years (with zero efficacy beyond those timepoints) would be informative (ATAGI Advice, March 2025).

6.58 The PSCR argued that it would be implausible to assume no residual protection beyond the available trial follow-up, stating the relatively slower waning observed in the trial data between Seasons 2 and 3 compared with Seasons 1 and 2 indicates plausible vaccine efficacy beyond 3 years.

6.59 The ESC recalled that, in its November 2024 consideration of RSVPreF, the PBAC had considered the VE for RSVPreF should be truncated at 2 years based on the RENOIR study which had an average follow up of 1.4 years (16.4 months) (paragraph 7.16, RSV

vaccine Abrysvo PSD, November 2024 PBAC meeting). The ESC considered that, based on the available data, it would be reasonable to assume a longer period of VE for RSVPreF3 OA (i.e. longer than 2 years) given the duration of trial follow-up for AReSVi-006 was a median of 30.6 months, with the trial designed to assess VE up to the end of Season 3. The ESC noted that the duration and magnitude of effect beyond the trial period (after Season 3) is unknown and that it may be reasonable to consider truncating the VE of RSVPreF3 OA at 3 or 4 years. The ESC also noted that the modelled benefit from a single dose would not be realised in clinical practice, if revaccination is recommended (in the future) earlier than the year of truncation in the model. Thus, if the assumed duration of VE is greater than the window for revaccination, the cost-effective price for RSVPreF will be overestimated. In relation to this, the ESC noted that revaccination at 3 and 4 years is being assessed in the clinical studies (refer to paragraph 6.40).

6.60 A summary of the RSV-associated hospitalisation rates for adults ≥75 YOA applied in the economic model is presented in Table 15. The applied estimate for RSV-associated hospitalisation rates in the resubmission is higher than the rates previously accepted by the ATAGI and PBAC.

Table 15: RSV-associated hospitalisation rates for the ≥ 75 YOA in the resubmission (per 100,000 person-years)

Age (years)	*July 2025 PSCR*		July 2025 resubmission		July 2024 submission	ATAGI Advice (March 2025) [b]		November 2024 RSVPreF PBAC recommendation
75-79	304	443 [a]	364	577 [a]	501	240	384 [a]	384 (accepted by the PBAC) [a,c]
80-84	556		750		501	495		
≥85	556		750		916	495		

Source: Compiled during the evaluation; Table 3-19, p204 of the resubmission; worksheet 'ResubUpdates' of the economic model from the resubmission; Table 40, p73, ATAGI Advice, March 2025; paragraph 7.16, RSVPreF PSD, November 2024; Table 2 of PSCR.
ATAGI = Australian Technical Advisory Group on Immunisation; RSVPreF = recombinant RSV prefusion F protein vaccine.
[a] Weighted by population size of each age category from the resubmission i.e. using a population weighting of: 45% 75-79 YOA; and 55% 80+ YOA. This weighted estimate is for comparison purposes, as the resubmission used rates per age band for the economic model.
[b] Per the ATAGI advice based on a multiplication function of 2.0 (Table 40, p73, ATAGI Advice, March 2025).
[c] Per the ATAGI advice (paragraph 6.54, and 7.16, RSVPreF PSD, November 2024). The original rate presented by the November 2024 RSVPreF submission was 398 per 100,000 person-years. Blue shading indicates data previously seen by the PBAC.

6.61 The resubmission's approach for adjusting RSV-associated hospitalisation rates was to use the 2016-2019 AIHW National Hospital Morbidity Database (NHMD) hospitalisation crude rate to which it applied 2 separate multipliers: one of 2.0 (noted as an under-testing correction) and another of 1.5 (noted as an under-ascertainment multiplier for test sensitivity based on 66% sensitivity of RT-PCR of nasopharyngeal swabs). This approach, specifically the application of the 1.5 multiplier, was inconsistent with previous advice from the ATAGI and PBAC. The ATAGI advised that the crude AIHW NHMD hospitalisation rate data should be used as the base case for unadjusted RSV-associated hospitalisation rates, and that applying a multiplication factor of 2.0 to these rates is appropriate (ATAGI Advice, March 2025). This multiplication factor of 2.0 was also recommended for RSVPreF submitted for PBAC's consideration in the November 2024 meeting by ATAGI and PBAC (paragraph 6.54 and

7.16, RSVPreF PSD, November 2024). The impact on the cost-effectiveness results of excluding the 1.5 multiplier is presented in sensitivity analyses.

6.62 The PSCR argued that the 2.0 multiplier does not completely account for the under-reporting of RSV hospitalisation cases. The PSCR considered that the RSV hospitalisation rates reported in the years closer to the onset of the COVID-19 pandemic (i.e. 2018-19) were under-estimated to a lesser extent (i.e. compared with the 2016–2019 AIHW data) due to improved RSV testing practices. As such, the PSCR presented a revised scenario analysis in which the 2.0 multiplier was applied to 2018-19 AIHW data (rather than a 2.0 multiplier and a 1.5 multiplier being applied to 2016-19 AIHW data). The resulting rates are shown in Table 15.

6.63 The ESC considered that the RSV-associated hospitalisation rate should align with the value previously recommended by the PBAC in its November 2024 consideration of RSVPreF (i.e. based on AIHW 2016-2019 data with a 2.0 multiplier), which was a rate of 240 per 100,000 in people aged 75-79 years, and 495 per 100,000 in people aged 80+ years (weighted average of 384 per 100,000 person-years for the ≥75 YOA population). The pre-PBAC response proposed that application of AIHW data from 2018-19 would be appropriate (i.e., exclusion of 2016-17 data), however the PBAC noted this advice was not consistent with the ATAGI pre-submission advice dated 7 March 2025 (see paragraph 6.81).

6.64 The resubmission estimated the RSV-associated hospitalisation rate for Aboriginal and Torres Strait Islander people to be 364 per 100,000 person-years for 60-64 YOA and 750 for 65-74 YOA (572 for 60-74 YOA, weighted by the population size of each age category). The evaluation noted that although these estimates were inconsistent with the ATAGI pre-submission advice to the PBAC (i.e., 240 for 60-64 YOA and 495 for 65-74 YOA;ATAGI Advice, March 2025), they are comparable with those in the RSVPreF submission considered at the PBAC November 2024 meeting (576 for 60-74 YOA; paragraph 7.18, RSVPreF PSD, November 2024). The PBAC previously stated that the rate estimated in the RSVPreF submission, which was consistent with advice provided by ATAGI (1.5 times the rate for ≥75 YOA years), was reasonable in the context of the relatively small population size (paragraph 7.18, RSVPreF PSD, November 2024). The PSCR for RSVPreF3 OA, in the revised base case analysis for the Aboriginal and Torres Strait Islander people aged 60–74 years population, applied a multiplier of 1.5 to the rate that it had estimated for the ≥75 YOA population (i.e. 443*1.5) to derive a hospitalisation rate of 665 per 100,000 people. However, the ESC considered that the RSV-associated hospitalisation rate in this population should align with the value previously recommended by the PBAC in its November 2024 consideration of RSVPreF in this same population (i.e. a weighted rate of 576 for Aboriginal and Torres Strait Islander people aged 60-74 years).

6.65 The resubmission applied the same baseline utility values obtained from Redwood et al. 2024 for both the ≥75 YOA and Aboriginal and Torres Strait Islander people 60–74 YOA. Aboriginal and Torres Strait Islander peoples generally report lower health-related quality of life than the Australian population norms. The PBAC also previously

noted a lower utility value applied for Aboriginal and Torres Strait Islander peoples in the RSVPreF submission (0.675 from Banham 2019; Table 11, RSVPreF PSD, November 2024); the impact of using the Banham 2019 utility value was tested in a sensitivity analysis during the evaluation. The PSCR applied the utility value from Banham 2019 (i.e. 0.675) in its revised scenario analysis for Aboriginal and Torres Strait Islander people aged 60-74 years, consistent with the RSVPreF PSD from November 2024.

6.66 A summary of the updated RSV-associated hospitalisation costs presented in the resubmission compared to those previously seen by the PBAC is presented in Table 16. The updated cost in the resubmission was estimated at $20,091, which was similar to the value the ESC considered was an overestimate in the July 2024 submission. With respect to the July 2024 submission, the ESC suggested a hospitalisation cost of $9,219 (paragraph 6.68, RSVPreF3 OA PBAC Minutes, July 2024); similarly, the PBAC accepted a hospitalisation cost of $8,542 for the RSVPreF submission (Table 11, RSVPreF PSD, November 2024).

Table 16: Estimated RSV-associated hospitalisation costs in the resubmission compared to previous submissions and November 2024 RSVPreF submission

	July 2025 resubmission	July 2024 submission and evaluation			November 2024 RSVPreF PBAC recommendation
		July 2024 submission	July 2024 submission's PSCR	Evaluation/ESC	
Hospitalisation cost per case	≥ 75 YOA: $20,091 PSCR: tested estimates of $15,525 to $16,693.	75-79 YOA: $20,578 ≥ 80 YOA: $22,713	New base case: 75-79 YOA: $21,995 ≥ 80 YOA: $24,277 Scenario A: 75-79 YOA: $15,137 ≥ 80 YOA: $16,707 Scenario B: 75-79 YOA: $14,803 ≥ 80 YOA: $16,338	≥ 60 YOA: $9,219	≥ 60 YOA: $8,542 (accepted by the PBAC)
Source	Hitch et al. 2024 PSCR: based on AR-DRG costs inflated by 50%, Hitch et al 2024 (lower confidence interval, not adjusted for inflation) and Brusco et al 2022	NEP: 2023, NHCDC cost weights & separations: 2019-20, AR-DRG: E62A-B	NEP: 2024, NHCDC cost weights & separations: 2020-21, AR-DRG: E62A-B	Based on the July 2024 submission's PSCR but removing adjustment for ICU and LOS	AR-DRG: E62A-B, NHCDC for 2020-21, 2023 values

Source: Worksheet 'ResubUpdates' of the July 2025 resubmission's economic model; para 6.68, Table 16, and Table 24, RSVPreF3 OA, PBAC Minutes, July 2024 PBAC meeting; Table 11, RSVPreF PSD, November 2024.
AR-DRG = Australian Refined Diagnosis Related Groups; ESC = Economics Sub-Committee; NEP = national efficient price; NHCDC = National Hospital Cost Data Collection; PSCR = pre-subcommittee response; YOA = years of age
Blue shading indicates data previously seen by the PBAC.

6.67 The resubmission stated that the hospitalisation costs ($9,219) previously advised by the ESC were considerably underestimated. The resubmission referenced Brusco et al. 2022 (N = 363, Murdoch Children's Research Institute; MCRI in Melbourne), which estimated the hospitalisation cost in children under 5 years to be $12,589 in 2018, equating to $16,239 in 2024/25 value. The resubmission also stated that RSV-related hospitalisations typically incur higher costs for older adults than children (Amand et

al. 2018 and McRae et al. 2023). The evaluation considered that this might be reasonable given that RSV hospitalisations in older adults are significant in terms of length of stay. However, one recently published Australian cost-effectiveness study identified during the evaluation (Nazareno et al. 2025) suggests that overall hospitalisation costs exhibit a U-shaped pattern (rather than linearity), with higher costs observed in the youngest age group (< 5 years) and those aged ≥ 45 years, while costs are lower for individuals aged 5-34 years. Specifically, children under 5 years incur hospitalisation costs comparable to those aged ≥75 years. Limited further evidence is available as to whether hospitalisation costs increase with age.

6.68 The revised hospitalisation costs in the resubmission ($20,091) were sourced from Hitch et al. 2024. The study is a cost comparison analysis of hospital admissions due to COVID-19 or other viral pneumonias between 1 January 2020 and 30 June 2021 at Victorian public health acute and subacute services (Victorian Admitted Episodes Dataset; VAED)). The direct cost from "other viral pneumonias" (n = 15,716) was chosen to represent the RSV-associated hospitalisation costs in the economic model (adjusted to 2024 price). The study's primary aim was to understand the economic impact of COVID-19. The inclusion of other viral pneumonias serves to contextualise the costs associated with COVID-19, not to provide a detailed cost analysis of each specific type of viral pneumonia like RSV. The evaluation considered that it was unclear whether the cost of viral pneumonia hospitalisation is a good proxy for RSV-associated hospitalisation costs. Further, the cost was substantially higher than the cost included in the submission for RSVPreF that was considered at the November 2024 PBAC meeting of $8,542.

6.69 The PSCR tested three other hospitalisation costs in scenario analyses:

- $15,525, based on AR-DRG cost weights (E62A and B) inflated by 50% based on expert opinion. The PSCR argued that the weighted mean length of stay for E62A and E62B is 4.4 days, which is lower than the actual RSV length of stay reported for > 75 YOA (mean: 6.8 to 8 days; AIHW NHMD 2012-19, NCIRS analysis). However, the ESC did not accept the PSCR's proposed inflation of the cost by 50% based on expert opinion rather than evidence.
- $16,125, based on Hitch et al. 2024 (per the submission base case), but applying the lower confidence interval for viral pneumonia, not adjusted for inflation; and
- $16,693 based on Brusco et al. 2022 (patient-level data in children <5 years).

These updated hospitalisation costs are lower than those used in the resubmission ($20,091), but higher than both the ESC's advised cost for the July 2024 submission ($[redacted]) and the cost accepted by the PBAC for the RSVPreF November 2024 submission ($8,542 based on AR-DRG E62A and E62B, NHCDC 2020-21 updated to 2023 values). The ESC noted the values presented in both the submission and the PSCR were not the applicable population and condition (i.e. they were studies conducted in children, or assessing 'other viral pneumonias') or were based on expert opinion. The ESC considered that these studies may not represent more reliable estimates of RSV-

associated hospitalisation costs in the applicable population than AR-DRG cost weights, noting these already account for more severe cases.

6.70 Overall, the ESC considered that it may be reasonable for the hospitalisation cost to align with the value previously recommended by the PBAC in its November 2024 consideration of RSVPreF in this same population i.e. $8,542. Based on 2025 data, the comparable hospitalisation cost would be $9,900 (paragraph 7.14).

6.71 The pre-PBAC response proposed a hospitalisation cost of $12,510 based on E62A (NHCDC 2020 – 2021 adjusted to 2025 value) The resubmission updated the RSV-related death probability from the Tseng et al. 2020 US-based study (10.87% for ≥75 YOA) used in the previous submission for the ≥75 YOA population to hospital case fatality data from the AIHW NHMD 2012-2019 (3.29% for 75-79 YOA, and 4.55% for ≥80 YOA), as per the ATAGI Advice (ATAGI Advice, March 2025). A comparable RSV-hospital case fatality rate from the ATAGI (4.22% for ≥75 YOA) was recommended by the PBAC for the RSVPreF submission (paragraph 7.16, RSVPreF PSD, November 2024). The resubmission noted potential issues with using the hospitalisation rates from the AIHW NHMD 2012-2019 data, including the under-ascertainment of case fatality rates and potential inaccuracies in coding, which might result in underestimating RSV-related death. ATAGI proposed sensitivity analyses be conducted for the in-hospital case fatality rate, with an upper bound of 8.00% (paragraph 6.56, RSVPreF PSD, November 2024). The revised scenario analysis presented in the PSCR applied an RSV-hospital case fatality rate of 4.22% to the model for the population aged ≥75 years, i.e. as recommended by the PBAC for the RSVPreF submission.

6.72 The resubmission applied the same RSV-related death probability that was used in the ≥75 YOA population (the AIHW NHMD 2012-2019) to the Aboriginal and Torres Strait Islander people 60-74 YOA population, using the corresponding age group's RSV-related death probability (2.57% for 60-64 YOA, 3.26% for 65-69 YOA, and 3.60% for 70-74 YOA). The ATAGI noted that it is likely that the RSV-hospital case fatality rate would be higher in this population, and that in the absence of more granular data on this parameter, applying the rate for ≥75 YOA (4.22%) to Aboriginal and Torres Strait Islander people (aged from 60 years), allows for a moderate increase in the death probability above that of the general population (ATAGI Advice, March 2025). The impact on the cost-effectiveness results of applying the death rate for ≥75 YOA (4.22%) to Aboriginal and Torres Strait Islander people 60-74 YOA is presented in a sensitivity analysis. The RSV-hospital case fatality rate was unchanged in the scenario analysis presented in the PSCR for the Aboriginal and Torres Strait Islander people 60-74 YOA population.

6.73 A summary of the key drivers of the model is presented in Table 17.

Table 17: Key drivers of the model (submission base case)

Description	Method/Value in submission base case	Impact vs submission base case
≥75 YOA		**Base case: $[redacted][3]/QALY gained**
Under-ascertainment multipliers	Including 2.0 and 1.5 multipliers to 2016-2019 AIHW NHMD hospitalisation crude rates	High, favours RSVPreF3 OA Excluding the 1.5 multiplier increased the ICER to $[redacted][1]/QALY gained.
Hospitalisation cost	Using direct costs for treating viral pneumonias obtained from Hitch et al. 2024	High, favours RSVPreF3 OA Use ≤ 5 YOA costs ($16,239) per Brusco et al. 2022 increased the ICER to $[redacted][2]/QALY gained.
Waning	2-year waning convergence to 0 at year 5	High, favours RSVPreF3 OA Use 1-year linear logarithmic waning, convergence to 0% at year 4 increased the ICER to $[redacted][3]/QALY gained.
RSV-related death	Using AIHW NHMD 2012-2019 data (3.29%; 75-79 YOA, and 4.55%; ≥80 YOA)	High, favours no vaccine Use of ATAGI's suggested upper bound rate (8.00%) for a sensitivity analysis decreased the ICER to $[redacted][4]/QALY gained.
Aboriginal and Torres Strait Islander people 60-74 YOA		**Base case: $[redacted][2]/QALY gained**
Hospitalisation cost	Using direct costs for treating viral pneumonias obtained from Hitch et al. 2024	High, favours RSVPreF3 OA Use ≤ 5 YOA costs ($16,950) per Brusco et al. 2022 increased the ICER to $[redacted][1]/QALY gained.
Waning	2-year waning convergence to 0 at year 5	Moderate/high, favours RSVPreF3 OA Use 1-year linear logarithmic waning, convergence to 0% at year 4 increased the ICER to $[redacted][5]/QALY gained.
RSV-related death	Using AIHW NHMD 2012-2019 data (2.57%; 60-64 YOA, 3.26%; 65-69 YOA, 3.60%; 70-74 YOA)	High, favours no vaccine Use ATAGI's suggested upper bound rate (8.00%) for a sensitivity analysis decreased the ICER to $[redacted][3]/QALY gained.

Source: Compiled during the evaluation.

AIHW = Australian Institute of Health and Welfare; ATAGI = Australian Technical Advisory Group on Immunisation; ICER = incremental cost-effectiveness ratio; NHMD = National Hospital Morbidity Database; PBAC = Pharmaceutical Benefits Advisory Committee; QALY = quality-adjusted life year; RSV= respiratory syncytial virus; YOA = years of age.

The redacted values correspond to the following ranges:

[1] *$35,000 to < $45,000*

[2] *$15,000 to < $25,000*

[3] *$5,000 to < $15,000*

[4] *$0 to < $5,000*

[5] *$25,000 to < $35,000*

6.74 A summary of the results of the economic evaluation from the resubmission is presented in Table 18.

Table 18: Results of the economic evaluation

	No vaccine	RSVPreF3 OA	Incremental difference
Adults ≥75 YOA			
Population	[redacted][1]	[redacted][1]	0
Vaccinated population	0	[redacted][1]	[redacted][1]
Direct costs	$1,170,646,212	$[redacted]	$[redacted]
LYs lost	14,219	7,518	-6,701
QALYs lost	17,863	10,054	-7,808
Cost per LY gained			$[redacted][3]
Cost per QALY gained			**$**[redacted][4]
PSCR [a]			
Cost per QALY gained with hospital costs $20,091			**$**[redacted][a4]
Cost per QALY gained with hospital costs $15,525 to $16,693			**$**[redacted][3] **to $**[redacted][3]
Previous PBAC July 2024 consideration			
Incremental cost per QALY gained			**$**[redacted][3]
Incremental cost per QALY gained (revised base case from the PSCR)			**$**[redacted][4]
Aboriginal and Torres Strait Islander people 60-74 YOA			
Population	[redacted][5]	[redacted][5]	0
Vaccinated population	0	[redacted][5]	[redacted][5]
Direct costs	$30,477,143	$[redacted]	$[redacted]
LYs lost	215	110	-105
QALYs lost	340	191	-149
Cost per LY gained			$[redacted][6]
Cost per QALY gained			**$**[redacted][7]
PSCR [b]			
Cost per QALY gained with hospital costs $20,091			**Dominant**
Cost per QALY gained with hospital costs $15,525 to $16,693			**Dominant to $**[redacted][4]

Source: Table 3-65, p248 of the resubmission; Table 6.71, para 6.84, RSVPreF3 OA, PBAC Minutes, July 2024 PBAC meeting.
LY = life years, PSCR = Pre-subcommittee response; QALY = quality-adjusted life year, YOA = years of age.
Blue shading indicates data previously seen by the PBAC.
[a] PSCR Updated inputs: new proposed price, revised hospitalisation rate, revised hospitalisation costs, and applying parameters used in the RSVPreF submission ($7.00 administration cost and 4.22% RSV related-death rate).
[b] PSCR updated inputs: new proposed price, revised hospitalisation rate, revised hospitalisation costs, and applying parameters used in the RSVPreF submission ($7.00 administration cost, 0.67 baseline utility).
The redacted values correspond to the following ranges:
[1] *2,000,000 to < 3,000,000*
[2] *< 500*
[3] *$5,000 to < $15,000*
[4] *$0 to < $5,000*
[5] *70,000 to 80,000*
[6] *$35,000 to < $45,000*
[4] *$15,000 to < $25,000*

6.75 In the submission base case, the ICERs differed between the ≥75 YOA population, with$5,000 to < $15,000 per QALY gained, and the Aboriginal and Torres Strait Islander peoples 60-74 YOA, with $15,000 to < $25,000 per QALY gained. The PBAC previously noted that given the increased rate of hospitalisation in Aboriginal and Torres Strait Islander people (and other high-risk individuals), it would be expected that RSVPreF3 OA would be associated with lower incremental costs and higher incremental QALYs and LYs in these populations. However, the impact of other population characteristics

on cost-effectiveness is uncertain (e.g., the impact of comorbidities affecting survival in the population, which may lead to increased ICERs) (paragraph 6.45, RSVPreF3 OA PSD, July 2024). The results from the resubmission, where the ICER is more favourable in the ≥ 75 YOA population than in Aboriginal and Torres Strait Islander people 60-74 YOA, are contrary to such expectations. This is explained by the resubmission applying overestimated hospitalisation rates to the ≥75 YOA population. Additionally, the less favourable results for the Aboriginal and Torres Strait Islander people 60-74 YOA group are explained by their higher background mortality rates compared to those of the ≥75 YOA population.

6.76 The ESC previously noted that vaccine cost-effectiveness had a strong age gradient, and that presenting the results in age bands would be required for decision-making (paragraph 6.88, RSVPreF3 OA PSD, July 2024). Accordingly, a summary of the results for the ≥ 75 YOA population in age bands is presented in Table 19, based on the submission base case. Similar to the previous submission, the cost-effectiveness of the vaccine continues to show a strong age gradient, though the ESC considered the age gradient was less relevant given the resubmission was not requesting listing in the population aged 60-74 years with risk factors.

Table 19: Results of the economic evaluation of the ≥ 75 YOA population per age group in five-year categories (based on the submission base case): based on submission model

Age group (YOA)	Population	RSV-LRTD hospital.	30-day mortality within hospital admission	Possibility of death given RSV-LRTD	Inc. costs	Inc. QALYs	ICER	ICER (July 2024)
75-79	[redacted][1]	19.3%	3.29%	0.64%	$[redacted]	3,331	$[redacted][2]	$[redacted][3]
80-84	[redacted][3]	39.8%	4.55%	1.81%	-$[redacted]	3,684	Dominant	$[redacted][3]
≥85-89	[redacted][4]			1.81%	-$[redacted]	1,960	Dominant	Dominant

Source: Table 3-22, p207; Table 3-47, p232 of the resubmission; Attachment 'RSV OA static model_v16_PBAC_FINAL_March_2025'
Inc = incremental; ICER = incremental cost-effectiveness ratio; LRTD = lower respiratory tract disease; QALY = quality-adjusted life years; RSV = respiratory syncytial virus; RSVPreF3 OA= RSV Pre-fusion protein 3 older adult; YOA = years of age.
Blue shading indicates data previously seen by the PBAC.
The redacted values correspond to the following ranges:
[1] *1,000,000 to < 2,000,000*
[2] *$25,000 to < $35,000*
[3] *$5,000 to < $15,000*
[4] *600,000 to < 700,000*
[5] *300,000 to < 400,000*

6.77 The results of key univariate / multivariate sensitivity analyses are summarised in Table 20, based on the PSCR's economic model. As the PSCR proposed three scenario analyses using different hospitalisation costs, the sensitivity analyses in Table 20 are based on the cost of $16,125 (the intermediate of the three hospitalisation costs proposed in the PSCR).

Table 20: Sensitivity analyses based on PSCR model

Analysis	Inc. costs	Inc. QALYs	ICER
Adults ≥75 YOA (based on population size of [redacted][1] in each arm)			
Base case	$[redacted]	6,699	$[redacted][2]

Analysis	Inc. costs	Inc. QALYs	ICER
Discount rate: 3.5% (base case: 5%)	$ [redacted]	7,204	$ [redacted][2]
Discount rate: 0% (base case: 5%)	$ [redacted]	8,748	$ [redacted][2]
VE and waning (base case: 3-year logarithmic model + 2-year linear waning, converges to 0% at year 5)			
A.3-year logarithmic model	$ [redacted]	5,785	$ [redacted][3]
B.3-year logarithmic model + 1-year linear wanning (VE to 0% at year 4)	$ [redacted]	6,247	$ [redacted][3]
RSV-associated hospitalisation rates (base case in PSCR: 443 per 100,000 person-years for ≥75 YOA)			
C. ATAGI pre-submission advice to PBAC March 2025: 384 per 100,000 person-years	$ [redacted]	5,995	$ [redacted][3]
RSV-hospital case fatality rate (base case in PSCR: 4.22%)			
ATAGI's advised upper bound for a sensitivity analysis (8.00%)	$ [redacted]	10,862	$ [redacted][2]
RSV-associated hospitalisation costs (PSCR: $15,525 to $16,693)			
D. Hospitalisation costs per RSVPreF November 2024 submission ($8,542)	$ [redacted]	6,699	$ [redacted][4]
Multivariate sensitivity analyses (PSCR model)			
C+D: Hospitalisation rate of 384 per 100,000 person-years, $8,542 hospitalisation costs (VE over 5 years)	$ [redacted]	6,361	$ [redacted][5]
B+C+D: Hospitalisation rate of 384 per 100,000 person-years, $8,542 hospitalisation costs and VE over 4 years	$ [redacted]	5,925	$ [redacted][5]
A+C+D: Hospitalisation rate of 384 per 100,000 person-years, $8,542 hospitalisation costs and VE over 3 years	$ [redacted]	5,483	$ [redacted][6]
PSCR base case (with hospital costs of $20,091, and VE of 5 years)	$ [redacted]	294	$ [redacted][7]
PBAC Scenario: PSCR model with hospital costs reduced from $20,091 to $9,900[a] and ED costs from $1,565 to $1,457[b], hospitalisation rate reduced from 443 to 384[c] (also reduces deaths in the model as mortality is a proportion of hospitalisations) and VE of 3 years, and RSVPreF3 OA price of $[redacted] as proposed in pre-PBAC response	$ [redacted]	241	$ [redacted][4]
Aboriginal and Torres Strait Islander people 60-74 YOA (based on population size of [redacted][8] in each arm)			
Base case	-$ [redacted]	140	Dominant
Discount rate: 3.5% (base case: 5%)	-$ [redacted]	148	Dominant
Discount rate: 0% (base case: 5%)	-$ [redacted]	171	Dominant
VE and waning (base case: 3-year logarithmic model + 2-year linear waning, convergence to 0% at year 5)			
3-year logarithmic model	$ [redacted]	123	$ [redacted][2]
3-year logarithmic model + 1-year linear wanning (VE to 0% at year 4)	$ [redacted]	132	$ [redacted][6]
RSV-associated hospitalisation costs (PSCR: $15,525 to $16,693)			
Hospitalisation costs per RSVPreF November 2024 submission ($8,542)	$ [redacted]	140	$ [redacted][4]
RSV-associated hospitalisation rates (base case in PSCR: 665 per 100,000 person-years)			
576 per 100,000 person-years	$ [redacted]	129	$ [redacted][2]
RSV-hospital case fatality rate (base case: 2.57% for 60-64 YOA increasing to 4.55% for 80+ YOA)			
ATAGI's advised upper bound for a sensitivity analysis (8.00%)	-$ [redacted]	284	Dominant
ATAGI's advised 4.22% of ≥ 75 YOA applied to Aboriginal and Torres Strait Islander people 60-74 YOA population	-$ [redacted]	177	Dominant
Background mortality (base case: Aboriginal and Torres Strait Islander people specific mortalities)			
Assumed general population equivalence	-$ [redacted]	299	Dominant
Multivariate			
VE 5 years, with parameters for RSVPreF November 2024 submission (hospitalisation rate of 576 per 100,000 person-years, 4.22% RSV-hospital case fatality rate, $8,542 hospitalisation costs) [d]	$ [redacted]	161	$ [redacted][5]
VE 3 years (logarithmic), with parameters for RSVPreF November 2024 submission (hospitalisation rate of 576 per 100,000 person-years, 4.22% RSV-related death probability, $8,542 hospitalisation costs) [d]	$ [redacted]	141	$ [redacted][6]

Analysis	Inc. costs	Inc. QALYs	ICER
VE 4 years (3-year logarithmic model VE + 1-year linear wanning, convergence to 0% at year 4), with parameters for RSVPreF November 2024 submission (hospitalisation rate of 576 per 100,000 person-years, 4.22% RSV-related death probability, $8,542 hospitalisation costs) [d]	$[redacted]	151	$[redacted][6]

Source: Conducted during the evaluation using the economic models presented in the PSCR.
AIHW = Australian Institute of Health and Welfare; ATAGI = Australian Technical Advisory Group on Immunisation; ESC = Economic Sub-Committee; ICER = incremental cost-effectiveness ratio; Inc = incremental; LRTD = lower respiratory tract disease; NHMD = National Hospital Morbidity Database; N/R = not reported; PBAC = Pharmaceutical Benefits Advisory Committee; PSCR = Pre-sub-committee response; PSD = public summary document; QALYs = quality-adjusted life years; RSV = respiratory syncytial virus; VE = vaccine efficacy; YOA = years of age.

a. Hospital costs ($9,900) derived from NHCDC 2021/22 dataset, updated inflation to March 2025 Australian dollars using the current health subgroup CPI. Average cost weight for AR-DRG items E62 A/B, NHCDC 2021/22 ($8,480) inflated to March 2025.
b. ED costs ($,1457) derived from NHCDC 2021/22 dataset, updated inflation to March 2025 Australian dollars using the current health subgroup CPI. Average cost weight for AECC items E0450 A/B/C, (NHCDC) 2021/22 ($1,248) inflated to March 2025.
c. Hospitalisation rate reduced to 384 consistent with previous PBAC advice.
d. Table 11, paragraph 6.60 and 6.71, RSVPreF PSD, November 2024.

The redacted values correspond to the following ranges:
[1] 2,000,000 to < 3,000,000
[2] $5,000 to < $15,000
[3]$15,000 to < $25,000
[4] $25,000 to < $35,000
[5] $35,000 to < $45,000[6]$45,000 to < $55,000[7] $0 to < $5,000
[8] 70,000 to < 80,000

6.78 Using the PSCR's base case and applying some key inputs consistent with those recommended by the PBAC in November 2024 in its consideration of RSVPreF for the ≥75 YOA population (hospitalisation rate of 384 per 100,000 person-years and $8,542 hospitalisation costs; Table 11, paragraph 6.60 and 6.71, RSVPreF PSD, November 2024) increased the ICER to $35,000 to < $45,000 per QALY gained. Similarly, applying parameters consistent with those recommended by the PBAC in November 2024 in its consideration of RSVPreF for Aboriginal and Torres Strait Islander people 60-74 YOA (hospitalisation rate of 576 per 100,000 person-years, 4.22% RSV hospital fatality rate, and $8,542 hospitalisation costs; Table 11, paragraph 6.60 and 6.71, RSVPreF PSD, November 2024) increased the ICER to $35,000 to < $45,000 per QALY.

6.79 The submission did not present a cost-minimisation analysis comparing RSVPreF3 OA with RSVPreF. However, the resubmission presumed that cost-minimisation for the proposed vaccine, relative to RSVPreF (recommended by PBAC in November 2024), would be recommended by the PBAC if it deems RSVPreF3 OA to be non-inferior to RSVPreF. In such a case, the resubmission proposed that the equi-effective dose would be 1 dose of RSVPreF3 OA is equivalent to 1 dose of RSVPreF. However, the PSCR stated that the PBAC recommended price for RSVpreF informed by the end of Season 2 analysis (November 2024 PBAC recommendation) should not extend to RSVPreF3 OA (end of Season 3 analysis - March 2025 re-submission) using a cost minimisation framework because it is inconsistent with the available clinical evidence (paragraph 6.45). The PSCR stated that the cost effectiveness of RSVPreF3 OA and RSVPreF should be informed by cost utility analyses based on the respective evidence base for each vaccine. However, the ESC considered that, if separate cost-utility analyses were to be

used, then key assumptions such as baseline risk and hospitalisation rates and costs should align.

6.80 The pre-PBAC response provided a new model which extrapolated VE using a logarithmic function to 4 years, rather than 3 years as applied in the resubmission and PSCR. The pre-PBAC response claimed that it was reasonable to extend the linear logarithmic extrapolation of VE to 4 years with linear convergence to 0% at 5 years, [redacted] (paragraph 6.41). The PBAC considered this was not appropriate, instead advising that VE should be limited to 3 years in the model, consistent with available clinical data for RSVPreF3 OA (based on AReSVi-006 results for 3 seasons). Other amendments proposed in the pre-PBAC response were considered by the PBAC but not accepted because the PBAC considered that, key inputs should align with the accepted parameters for RSVpreF, such as baseline risk and hospitalisation rates and costs (refer PBAC Scenario in Table 20).

6.81 The pre-PBAC response referred to additional advice provided by the ATAGI RSV/respiratory working groups for the purposes of developing a model to inform program advice for the use of RSV vaccines in older adults (dated 19 December 2024), however this advice does not supersede the specific pre-submission advice dated 7 March 2025 provided to support the current PBAC consideration of RSVPreF3 OA (paragraph 2.6). The PBAC noted that exclusion of 2016-17 data from the estimates was not consistent with the ATAGI pre-submission advice dated 7 March 2025 (see paragraph 6.63).

RSVPreF3 OA cost per person

6.82 The intervention costs per patient are presented in Table 21 using the price proposed in the pre-PBAC response.

Table 21: Vaccine cost per patient (PSCR)

	Trial dose and duration	Economic Model	Financial estimates
Mean dose	1 dose	1 dose	1 dose
Mean duration	One-off[a]	One-off	One-off
Vaccine acquisition	$[redacted]	$[redacted]	$[redacted]
Administration fee	$7	$7	$7
Cost/person/course	$[redacted]	$[redacted]	$[redacted]

Source: p26 and 268 of the resubmission and Table 3-39, p225 of the resubmission; Tables 4 and 5 of the PSCR, and pre-PBAC response.
RSVPreF3 OA= RSV Pre-fusion protein 3 older adult.
[a] AReSVI-006 randomised participants at Year 2 to receive a Dose 2 and Dose 3 at 12 and 24 months, respectively, following the initial vaccination. As no significant differences were observed between the initial dose and Doses 2 and 3, a protocol amendment was implemented to discontinue Dose 3.

Estimated NIP usage & financial implications

6.83 This resubmission was not considered by DUSC.

6.84 The resubmission presented the financial impact of introducing a single dose of RSVPreF3 OA onto the NIP for adults: ≥75 YOA; and Aboriginal and Torres Strait

Islander people 60-74 YOA. This was consistent with the economic model and the requested NIP listing.

6.85 The resubmission used an epidemiological approach to estimate the eligible population.

6.86 The resubmission relied on the results of the economic model to account for the impact of RSVPreF3 OA VE including avoided cases of RSV-ARI, RSV-LRTD, RSV-URTD, vaccine-related AEs and resource utilisation. However, some discrepancies were identified between the approaches taken in the economic and financial analyses, such as in the incidence of RSV and hospitalisation rates.

6.87 Key inputs used by the submission are presented in Table 22.

Table 22: Key inputs for financial estimates

Parameter	Value applied and source	Comment
Uptake rate *or* *'coverage'*	Adults ≥75 YOA Yr 1: [redacted]% Yr 2-5: increases by [redacted]% per year Yr 6: [redacted]% Aboriginal and Torres Strait Islander people 60-64 YOA Yr 1: [redacted]% Yr 2-5: increases by [redacted]% per year Yr 6: [redacted]% 65-74 YOA Yr 1: [redacted]% Yr 2-5: increases by [redacted]% per year **Yr 6: [redacted]%**	The uptake assumptions were consistent with those recommended in the March 2025 ATAGI advice for adults ≥ 75 YOA: [redacted]% by Year 6 (ATAGI advice, March 2025). The July 2024 submission based its uptake rates for adults ≥ 75 YOA (Y1: [redacted]% to Y6: [redacted]%) from the NCIRS Annual Immunisation coverage report for influenza (2022). No changes were applied to the vaccine uptake compared to the July 2024 submission in Aboriginal and Torres Strait Islander peoples.
Doses of RSVPreF3 OA	≥ 75 YOA Yr 1: [redacted][1] to Yr 6: [redacted][2] Aboriginal and Torres Strait Islander peoples 60-64 YOA Yr 1: [redacted][3] to Yr 6: [redacted][4]	The evaluation considered that the uptake rate was applied to the same static cohort each year, without accounting for individuals who were vaccinated in the previous year. The evaluation considered that this overestimated the eligible population and therefore the number of doses dispensed. The PSCR argued that the cumulative uptake rates applied relate to vaccination coverage (i.e. % of the eligible pool who have been vaccinated each year).
Assumptions relating to non-NIP costs		
RSV incidence	Based on an incidence rate of RSV of 5.72% and VE as per AreSVi-006 the number of RSV-LRTD cases prevented were: • Adults ≥75 YOA: [redacted][5] Aboriginal and Torres Strait Islander people 60-74 year: [redacted][4]	The evaluation considered that the baseline incidence of RSV used in the financial model was inappropriate and higher than that used in the economic evaluation (3.95%). Furthermore, the evaluation considered that the rate of 3.95% may itself be overestimated (paragraph 4.2). No changes were applied to the incidence rate compared to the July 2024 submission (5.72%), despite the evaluation for that submission indicating that this estimate was considered uncertain (paragraphs 4.5 and 6.53, RSVPreF3 OA PSD, July 2024).
Cost per case avoided RSV-LRTD	Included GP visits, specialist visits, RSV testing, pathology, x-rays, bronchodilators, ED visits, ambulance, hospitalisations (including ICU and MV), LTCF admissions, post-hospital GP, and antibiotics.	Consistent with economic model; however, the evaluation and the ESC considered that the hospitalisation costs (driver of the economic model and financial impact) were overestimated by the resubmission ($20,092), noting this is not a cost to the NIP.

Source: Table 4-3 p259-260 of the resubmission

GP = general practitioner, ED= emergency department; ICU = intensive care unit; LRTD = lower respiratory tract disease; LTCF = long-term care facility; MV = mechanical ventilation; NCIRS = National Centre for Immunisation Research and Surveillance; NIP = National

Immunisation Program; PSCR = Pre-Sub-Committee Response; RSV = respiratory syncytial virus; RSVPreF3 OA = RSV pre-fusion protein 3 older adult; Y = year; YOA = years of age.
Blue shading indicates data previously seen by the PBAC.
The redacted values correspond to the following ranges:
[1] *800,000 to < 900,000*
[2] *200,000 to < 300,000*
[3] *20,000 to < 30,000*
[4] *5,000 to < 10,000*
[5] *100,000 to < 200,000*

6.88 The evaluation considered that the estimated number of vials used by the eligible population (prevalent population aged ≥75 years in 2025 and turning 75 each year as of 2026) was overestimated because vaccinated individuals were not excluded from the eligible population in the subsequent years. This means that the same 'static' population for 2025 (e.g., 1,000,000 to < 2,000,000 individuals aged 75–79) and the new individuals turning 75 each year were multiplied by the corresponding uptake rate for the following years without adjusting for individuals who had already been vaccinated, and would reflect the cost of individuals receiving more than one vaccination over the 6-year period, rather than the single dose as requested by the submission. However, the PSCR stated that the uptake rates applied in the financial estimates reflect 'vaccination coverage' i.e. the percent of the eligible pool who have been vaccinated each year.

6.89 For the ≥75 YOA population, the resubmission revised the peak uptake in Year 6 from [redacted]% (in the July 2024 submission) to [redacted]%, assuming a linear interpolation between Year 1 and Year 6 (linear increase of [redacted]% per year). This approach was appropriate and consistent with the ATAGI advice (ATAGI advice March 2025). The uptake rates applied to Aboriginal and Torres Strait Islander people remained unchanged from the July 2024 submission. The evaluation considered that this was appropriate.

6.90 The estimated use and financial implications to the Federal Government, and the State and Territory Governments, for the ≥ 75 YOA population are presented in Table 23. The PSCR included revised estimates based on the revised price for RSVPreF3 OA and revised administration costs (and revised offsets for hospitalisations).

Table 23: Estimated use and financial implications in adults ≥ 75 YOA

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Predicted number of vials[a]	[redacted][1]	[redacted][2]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]
Estimated financial implications of RSVPreF3 OA						
NIP	$[redacted][4]	$[redacted][5]	$[redacted][5]	$[redacted][6]	$[redacted][6]	$[redacted][6]
NIP (PSCR)[b, c]	$[redacted][4]	$[redacted][7]	$[redacted][7]	$[redacted][7]	$[redacted][7]	$[redacted][5]
Vaccine administration	$[redacted][8]	$[redacted][8]	$[redacted][8]	$[redacted][8]	$[redacted][8]	$[redacted][8]
Vaccine administration (PSCR, corrected)	$[redacted][8]	$[redacted][8]	$[redacted][8]	$[redacted][8]	$[redacted][8]	$[redacted][8]
PBS [d]	-$[redacted][8]	-$[redacted][8]	-$[redacted][8]	-$[redacted][8]	-$[redacted][8]	-$[redacted][8]
MBS [e]	$[redacted][8]	-$[redacted][8]	-$[redacted][8]	-$[redacted][8]	$[redacted][8]	$[redacted][8]
Estimated cost to NIP, PBS and MBS – resubmission	$[redacted][8]	$[redacted][5]	$[redacted][5]	$[redacted][6]	$[redacted][6]	$[redacted][6]
Estimated cost to NIP, PBS and MBS - PSCR	$[redacted][4]	$[redacted][7]	$[redacted][7]	$[redacted][7]	$[redacted][7]	$[redacted][5]
Costs for hospitalisations, ambulances, Emergency Department visits (as estimated in the resubmission)						
Other Federal budgets [f]	-$[redacted][5]	-$[redacted][5]	-$[redacted][5]	-$[redacted][5]	-$[redacted][7]	-$[redacted][7]
Total Federal budgets	$[redacted][4]	-$[redacted][8]	-$[redacted][8]	$[redacted][8]	$[redacted][8]	$[redacted][9]
State and Territory Governments [g]	-$[redacted][6]	-$[redacted][10]	-$[redacted][10]	-$[redacted][6]	-$[redacted][5]	-$[redacted][5]
All budgets combined	$[redacted][4]	-$[redacted][10]	-$[redacted][10]	-$[redacted][6]	-$[redacted][7]	-$[redacted][11]
Previous submission July 2024 (≥ 75 YOA)[a]						
NIP	$[redacted][14] ($[redacted][14])	$[redacted][6] ($[redacted][10])	$[redacted][6] ($[redacted][10])	$[redacted][10] ($[redacted][12])	$[redacted][10] ($[redacted][12])	$[redacted][10] ($[redacted][13])
PBS	-$[redacted][8] (-$[redacted][8])	-$[redacted][8] (-$[redacted][8])	-$[redacted][8] (-$[redacted][8])	-$[redacted][8] (-$[redacted][8])	-$[redacted][8] (-$[redacted][8])	-$[redacted][8] (-$[redacted][8])

Source: Table 4-30, p274 of the resubmission and Table 31, RSVPreF3 OA PBAC Minutes, July 2024 PBAC meeting.
K = thousand; MBS = Medicare Benefit Schedule; NIP = National Immunisation Program; PBS = Pharmaceutical Benefit Scheme.
Cells shaded grey indicate those that are based on hospitalisations (and ambulances and Emergency Department visits). These will vary depending on the hospitalisation costs accepted in the economic evaluation.
[a] Corrected uptake application for the newly eligible cohort (2025-27) in the ≥ 75 YOA population are presented in brackets. The July 2024 submission incorrectly applied the uptake rates from the 60-64, 65-69, and 70-74 YOA cohort to the newly eligible patients turning 75 years from 2025, 2026, and 2027, respectively.
[b] PSCR: Revised price ($[redacted] per vial)
[c] In the financial estimates worksheet provided with the PSCR, the NIP costs appeared to be incorrect due to hard-coating of values in the '4.1.b results' worksheet Rows 607. NIP costs were corrected to be based on cost per vial multiplied by the predicted number of vaccines.
[d] PBS costs = Offsets for reduced use of antibiotics and bronchodilators
[e] MBS costs = costs of vaccine administration and vaccine-related AEs; Offsets for reduced GP visits (including post-discharge), specialist visits, RSV testing, pathology and X-rays.
[f] Assumed Federal Budget contribution (41%) for ambulance and long-term care facilities
[g] Offsets for ED visits and hospitalisations, assuming 58% of these costs would be funded by States and Territories.
The redacted values correspond to the following ranges:
[1] *800,000 to < 900,000*
[2] *100,000 to < 200,000*
[3] *200,000 to < 300,000*
[4] *$100 million to < $200 million*
[5] *$40 million to < $50 million*
[6] *$50 million to < $60 million*
[7] *$30 million to < $40 million*
[8] *$0 to < $10 million*
[9] *$10 million to < $20 million*
[10] *$60 million to < $70 million*
[11] *$20 million to < $30 million*
[12] *$70 million to < $80 million*
[13] *$80 million to < $90 million*

[14] *$200 million to < $300 million*

6.91 The submission estimated that the total cost to the NIP of listing RSVPreF3 OA in adults ≥75 YOA would be $50 million to < $60 million in Year 6, and a total of $400 million to < $500 million in the first 6 years of listing. The PSCR estimated that the total cost to the NIP in the first 6 years of listing would be $300 million to < $400 million for adults ≥75 YOA, using the revised price of $[redacted] per vial (reduced from $[redacted]).

6.92 The resubmission estimated that, over the first six years of NIP listing, 1,000,000 to < 2,000,000 RSV vaccines would be administered to patients aged 75+ years. The resubmission estimated, based on ABS data, that there are 2.28 million people in this age group in 2025 (with a further 500,000 to < 600,000 people estimated to turn 75 in over the first six years of listing, for a total of 2,000,000 to 3,000,000individuals). Thus, overall, the submission estimated that [redacted]% of individuals who were aged 75+ at any time during the forward estimates would be vaccinated in the first six years of listing.

6.93 The estimated use and financial implications to the Federal Government, and the State and Territory Governments, for Aboriginal and Torres Strait Islander people aged 60-74 are presented in Table 24.

Table 24: Estimated use and financial implications in Aboriginal and Torres Strait Islander people aged 60-74

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Predicted number of vials[a]	[redacted][1]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Estimated financial implications of RSVPreF3 OA						
NIP	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]
NIP (PSCR)[a]	*$[redacted][3]*	*$[redacted][3]*	*$[redacted]*	*$[redacted][3]*	*$[redacted][3]*	*$[redacted][3]*
PBS	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]
MBS	$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	$[redacted][3]	$[redacted][3]
Costs for hospitalisations, ambulances, Emergency Department visits (as estimated in the resubmission)						
Other federal budgets	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]
State and Territory Governments	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]
All budgets combined	$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]
Previous submission July 2024 (Aboriginal and Torres Strait Islander people aged 60-74 years)						
NIP	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]
PBS	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]

Source: Source: Table 2-30, p274 of the resubmission. Table 32, RSVPreF3 OA PBAC Minutes, July 2024 PBAC meeting.
K = thousand; MBS = Medicare Benefit Schedule; NIP = National Immunisation Program; PBS = Pharmaceutical Benefit Scheme.
[a] *PSCR: Revised price ($[redacted] per vial)*
The redacted values correspond to the following ranges:
[1] *20,000 to < 30,000*
[2] *5,000 to < 10,000*
[3] *$0 to < $10 million*

6.94 The total cost to the NIP of listing RSVPreF3 OA for Aboriginal and Torres Strait Islander people 60-74 YOA was estimated to be $0 to < $10 million in Year 6, and a total of $10 million to < $20 million in the first 6 years of listing. The PSCR estimated that the total cost to the NIP in the first 6 years of listing would be $10 million to < $20 million, using the revised price of $[redacted] per vial (reduced from $[redacted]).

6.95 The ESC noted the high cost to the NIP in the first year of RSVPreF3 OA listing compared with later years, with most of the cost offsets occurring due to reduced hospitalisations (shared cost between the Federal and State and Territory Governments).

Quality Use of Medicines

6.96 The resubmission presented additional post marketing activities that include:

- education of healthcare professionals.
- awareness campaigns helping educate consumers about RSV, including the development of culturally appropriate patient support materials for people with linguistically diverse backgrounds and dissemination of non-promotional RSV disease awareness information.
- consumer market research to understand consumers and inform development of disease awareness campaigns.
- resources to support patients prescribed RSVPreF3 OA to healthcare professionals.
- support to patient organisations and general quality use of medicines measures.

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

7 PBAC Outcome

7.1 The PBAC recommended that respiratory syncytial virus vaccine (Arexvy, RSVPreF3 OA) be a designated vaccine for the purposes of the *National Health Act 1953* for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus (RSV) for adults 75 years of age and above, and for Aboriginal and Torres Strait Islander peoples aged 60 to 74 years. The PBAC considered that the vaccine was superior to no vaccine in terms of effectiveness with an acceptable safety profile, however the duration and magnitude of protection in the requested populations remained uncertain. The PBAC noted the clinical evidence for RSVPreF3 OA over three seasons, and advised that it would be reasonable to accept vaccine efficacy (VE) over a period of three years for the purposes of the economic evaluation. The PBAC recalled that the near market comparator (RSVPreF, Abrysvo) was recommended for NIP listing at the November 2024 PBAC meeting for the same populations (people ≥75 years and Aboriginal and Torres Strait Islander peoples aged 60 to 74 years). The PBAC noted the limitations of the indirect comparison presented in the resubmission, including the different durations of trial follow-up available, and on balance concluded that RSVPreF3 OA was non-inferior to RSVPreF with respect to comparative effectiveness and safety. The PBAC advised that RSVPreF3 OA would be cost-effective if it were cost-minimised to RSVpreF. The PBAC considered, given the comparable effectiveness and

safety of the RSVPreF3 OA and RSVpreF vaccines, that the listing should not result in any additional net cost to Government.

7.2 The PBAC recommended the listing of RSVPreF3 OA on the basis that it should be available through the National Immunisation Program (NIP) under the circumstances specified in Section 8 below (adults aged 75 years and above, and Aboriginal and Torres Strait Islander peoples aged 60 to 74 years).

7.3 The PBAC considered RSVPreF3 OA would be cost-effective if it were cost-minimised against RSVpreF for the two recommended populations (adults aged ≥75 years, and Aboriginal and Torres Strait Islander peoples aged 60 to 74 years). The PBAC noted that a cost minimisation approach would result in the same price per dose for RSVPreF3 OA as for RSVpreF, consistent with the clinical conclusion of non-inferior effectiveness and safety. The PBAC considered the equi-effective doses were:

- One dose (120 micrograms) RSVPreF3 OA (Arexvy);
- One dose (120 micrograms) RSVPreF (Abrysvo).

7.4 The PBAC noted and welcomed the advice from the ATAGI that was provided to assist with its consideration of this resubmission. The PBAC noted that ATAGI advice supported NIP listing for three populations, that is all adults aged ≥75 years, Aboriginal and Torres Strait Islander peoples aged 60 to 74 years; and people aged 60 to 74 years with increased risk of severe RSV disease due to pre-defined risk conditions. Consistent with its previous advice, the PBAC considered there was a high clinical need for an effective vaccine for the three populations supported by the ATAGI. The PBAC noted that the third population would be addressed in a future resubmission.

7.5 The PBAC previously considered that there is a high clinical need for vaccines, such as RSVPreF3 OA vaccine, to reduce the risk of RSV in older adults, especially those aged over 75 years, Aboriginal and Torres Strait Islander people, and those vulnerable due to existing medical conditions (paragraph 7.4, RSVPreF3 OA PSD, July 2024). The PBAC noted the proposed listing of RSVPreF3 OA vaccine was supported by the consumer comments received for this resubmission.

7.6 The PBAC noted that a number of RSV vaccines and monoclonal antibodies are in development globally for prevention of RSV disease, and the clinical algorithm is changing following TGA registration and market launch of the first wave of these products in Australia, including RSVPreF3 OA, RSVPreF, and mRNA-1345 (mRESVIA).

7.7 The PBAC accepted the proposed clinical place for RSVPreF3 OA as a single dose for the two at-risk populations proposed by the submission. The PBAC noted the need for revaccination has not been established and that the ATAGI will make recommendations for subsequent doses when this is sought by the sponsor. The PBAC noted that alternate revaccination schedules up to Month 60 after initial vaccination are being assessed in ongoing clinical studies. The PBAC noted that if revaccination is requested in the future, this would impact cost-effectiveness and financial implications, and would require further PBAC consideration of the cost effective price

of the first and subsequent vaccine doses. The PBAC advised that if the assumed duration of VE in the economic model is greater than the window for revaccination, the cost-effective price for RSVPreF3 OA will be overestimated.

7.8 The PBAC noted that administration errors involving RSVPreF3 OA have been reported to the TGA[5]. The PBAC noted that unlike RSVpreF which is listed on the NIP for use as a maternal vaccine to protect infants from RSV, RSVPreF3 OA is not recommended during pregnancy. An increase in preterm births was observed compared to placebo after administration of an investigational unadjuvanted RSVPreF3 vaccine to 3,557 pregnant women in the RSV MAT-009 trial (paragraph 3.13, RSVPreF3 OA PSD, July 2024). The PBAC highlighted the need for quality use of medicines strategies to decrease the risk of incorrect administration of RSV prevention products including RSVPreF3 OA[4].

7.9 The PBAC previously considered the first submission's nomination of 'no vaccine' as main comparator was appropriate in the absence of any vaccine for RSV being currently available on the NIP (paragraph 7.11, RSVPreF3 OA PSD, July 2024). For the resubmission, the PBAC considered that RSVPreF was the main comparator as it was recommended for NIP listing at the November 2024 PBAC meeting.

7.10 The PBAC previously considered that the claim of superior comparative effectiveness was reasonable for the main comparison between RSVPreF3 OA and no vaccination, based on the randomised placebo-controlled trial AreSVi-006 and a supportive trial AreSVi-004, albeit with uncertainty regarding the duration of benefit given that VE waned over time (paragraphs 7.13 and 7.14, RSVPreF3 OA PSD, July 2024). The first submission was based on 2 seasons data VE; for the resubmission, an additional season of data was provided in the resubmission. The PBAC noted that the resubmission presented additional data from the AReSVi-006 trial corresponding to median follow-up of 30.6 months (see paragraph 7.10 below). The PBAC was satisfied that RSVPreF3 OA provides, for some patients, a significant improvement in efficacy over no vaccine based on the results of AReSVi-006.

7.11 The PBAC advised that it would be reasonable to accept VE over a period of three years based on three seasons of data for AreSVi-006. However, the PBAC maintained that the duration of benefit remained uncertain, and noted that VE against first occurrence of RSV-LRTD was 81% for Season 1, 61% for Season 2, and 47% for Season 3. For the Season 3 individual results, the lower bound of the 95% CI did not exceed the pre-defined effectiveness threshold of 20% for first occurrence of RSV-LRTD and severe RSV-LRTD.

7.12 The PBAC considered there was insufficient evidence to support a claim of superior effectiveness for either vaccine. Regarding the indirect clinical comparison of RSVPreF3 OA to RSVPreF, the PBAC acknowledged the limitations of the comparison

[5] https://www.tga.gov.au/news/safety-updates/correct-administration-rsv-vaccine-and-antibody-products#:~:text=About%20the%20administration%20errors,the%20administration%20errors%20outlined%20above.

include that it was unadjusted and unanchored, there were differences in outcome definitions between trials, and there were different durations of trial follow-up available. Based on current evidence, the PBAC concluded that RSVPreF3 OA was non-inferior to RSVPreF with respect to comparative effectiveness and safety (paragraphs 6.47 to 6.49).

7.13 The PBAC noted that the United States CDC's Advisory Committee on Immunization Practices (ACIP) has supported an assumption of 36 months of protection for the protein subunit RSV vaccines (including RSVPreF3 OA and RSVPreF) for older adults since October 2024[6][7], noting this was increased from the ACIP's previous recommendation of 24 months in June 2024.

7.14 In regard to the CUA provided in the resubmission, the PBAC advised it was reasonable to model vaccine efficacy over a period of three years in the economic model as discussed in paragraph 7.10, rather than 4 or 5 years as had been proposed by the sponsor. The PBAC considered that key inputs should align with the accepted parameters for RSVpreF, such as baseline risk and hospitalisation rates and costs (paragraph 6.80). The corresponding amendments to the PSCR model included reduction of hospital costs from $20,091 to $9,900 and ED costs from $1,565 to $1,457, hospitalisation rate reduced from 443 to 384 and VE of 3 years (refer PBAC Scenario in Table 20). The PBAC considered that RSVPreF3 OA would be cost-effective if the price was equal to the recommended price for RSVpreF.

7.15 The PBAC recalled that when recommending listing of RSVpreF in November 2024, it had advised specifications for acceptable cost-effectiveness for each population separately (Adults aged 75 years and above; and Aboriginal and Torres Strait Islander peoples aged 60 to 74 years). Consistent with this approach, the resubmission for RSVPreF3 OA included the two populations proposed for the NIP. However, when deliberating on the current proposal, the PBAC noted that usage of RSVPreF3 OA in Aboriginal and Torres Strait Islander peoples aged 60 to 74 years was estimated to be less than 5% of total utilisation in older adults, and given the uncertainties in modelling assumptions (paragraph 6.75), including burden of disease in Aboriginal and Torres Strait Islander peoples, considered it would be more appropriate to conduct the assessment of cost-effectiveness in the population of adults aged 75 years and above, and that this would provide an acceptable assessment of cost-effectiveness for the NIP listing in Aboriginal and Torres Strait Islander peoples aged 60 to 74 years.

7.16 The PBAC advised that the vaccine price determined from the cost-effectiveness evaluation for adults aged 75 years and above would also be considered cost-effective

[6] National Center for Immunization and Respiratory Diseases. RSV Vaccination in Adults: Work Group Interpretations. ACIP Meeting, 24 October 2024. https://www.cdc.gov/acip/downloads/slides-2024-10-23-24/06-RSV-Adult-Melgar-508.pdf

[7] National Center for Immunization and Respiratory Diseases. RSV Vaccination in Adults: Work Group Interpretations. ACIP Meeting, 16 April 2025. https://www.cdc.gov/acip/downloads/slides-2025-04-15-16/04-Ortega-Sanchez-Adult-RSV-508.pdf

for the proposed NIP listing for Aboriginal and Torres Strait Islander peoples aged 60 to 74 years as discussed in paragraph 7.15.

7.17 The PBAC did not change its view previously expressed in July 2024, regarding the high clinical need in high risk patients aged 60-74, however the PBAC was unable to assess if RSVPreF3 OA was cost-effective based on the information presented in the resubmission for this group (see paragraph 7.4). The PBAC noted that the costs to the NIP for this group had been estimated as more than $300 million to < $400 million over 6 years by the July 2024 submission (paragraph 6.108, RSVPreF3 OA PSD, July 2024).

7.18 The PBAC noted that the financial implications had been calculated using the proposed price in the PSCR, however the estimates would need to be recalculated using the cost-effective price recommended by the PBAC which was equal to the recommended price for RSVpreF. It was noted that the estimated volume of vaccinations in Year 1 was substantially higher than the following years, due to the large prevalent population above the relevant age thresholds, that will potentially come forward for vaccination in the first year after the NIP listing is implemented.

7.19 The PBAC noted that there would be no additional financial impact of listing RSVPreF3 OA on the NIP, as the recommended price was equal to the recommended price for RSVPreF.

7.20 The PBAC reiterated that the submission requested listing on the NIP for a single dose of vaccine and that if the sponsor wishes to request listing for revaccination in the future, PBAC consideration of a new submission would be required.

7.21 The PBAC noted that this submission is not eligible for an Independent Review because it is only relevant to submissions requesting a listing (or change to a listing) on the PBS.

Outcome:
Recommended

2 Recommended listing

2.1 Add new item to the Determination:

Vaccine and the circumstances in which vaccine may be provided	Brand	Formulation	Active ingredient and strength	Number and timing of doses
Vaccine respiratory syncytial virus (RSV) stabilised prefusion F protein vaccine ($AS01_E$ adjuvanted)	Arexvy	Injection (0.5mL)	Each 0.5mL dose contains 120 µg of RSVPreF3 antigen adjuvanted with GSK proprietary adjuvant system, $AS01_E$.	1 dose
Circumstances • Adults 75 years of age and above; • Aboriginal and Torres Strait Islander peoples aged 60 to 74 years.				

This restriction may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

9 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.

10 Sponsor's Comment

The sponsor had no comment.