5.08 mRNA-1273 mRNA COVID-19 vaccine Suspension for injection containing SARS-CoV-2 spike protein (mRNA), 50 micrograms (0.5 mL dose), Spikevax®, Moderna Australia Pty Ltd.

1 Purpose of submission

1.1 This Category 2 submission requested a National Immunisation Program (NIP) listing of mRNA-1273 (Spikevax®) for the prevention of coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 in four populations of adults as follows:

1) Adults aged 75 years or more (2 doses per year);
2) Adults aged 65-74 years (1 dose per year);
3) Adults aged 18-64 years with severe immunocompromise (1 dose per year); and
4) Aboriginal and Torres Strait Islander adults aged 50 to 74 years (1 dose per year).

1.2 Listing was requested on the basis of a cost-utility analysis comparing the Spikevax vaccine (variant updated messenger ribonucleic acid [mRNA]) to no vaccination. Table 1 summarises the key components of the Population, Intervention, Comparator, Outcomes (PICO) framework and the clinical claims presented in the submission. Primary doses were not requested for NIP listing.

1.3 The proposed NIP listing represents a restricted group in comparison to current arrangements under the National COVID-19 Vaccination Program (NCVP). The proposal did not request NIP listing for instances for which ATAGI has recommended to "consider" a dose based on individual risk-benefit assessment.

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

Component	Description
Population	Vaccination of age 18 years and older in accordance with the ATAGI recommended population and schedule: ○ 75 years and older: Every 6 months ○ 65–74 years: Every 12 months ○ 18–64 years with severe immunocompromise: Every 12 months ○ 50-64 years, Aboriginal and Torres Strait Islanders: Every 12 months.
Intervention	Spikevax vaccine updated for the most recent variant(s) of concern, TGA approved
Comparator	Main: • No vaccination TGA-approved near-market comparator: • Comirnaty vaccines (updated for the most recent variant of concern, TGA approved)
Outcomes	Effectiveness: • Vaccine effectiveness: Reducing the number of symptomatic COVID-19 cases, COVID-19 related medical attendance, COVID-19 related hospitalisation, COVID-19 related ICU admission and mortality Immunogenicity: • Immunogenicity: pseudovirus neutralising antibody (GM level) and seroprevalence (SRR) Safety: • Solicitated (local and systemic) adverse reactions within 7 Days After Injection • Unsolicited adverse events within 28 days after injection
Clinical claim	Main comparator: • Spikevax is superior compared to no updated vaccine in reducing the number of COVID-19 infections, COVID-19 related medical attendance, hospitalisation, ICU admission and mortality, and improving immunogenicity. Spikevax is well tolerated with an acceptable safety profile. Spikevax is inferior compared to no updated vaccine in terms of safety. TGA-approved near market comparator: • Spikevax is at least non-inferior to Comirnaty in reducing the number of COVID-19 infections, COVID-19 related hospitalisation and mortality, and improving immunogenicity. Spikevax is non-inferior compared to Comirnaty in terms of safety.

Source: Table 1.1, p18 and text p112 of the submission.
ATAGI = Australian Technical Advisory Group on Immunisation; COVID-19 = coronavirus disease 2019; GM = geometric mean; ICU = intensive care unit; SRR = seroreversion rates; TGA = Therapeutic Goods Administration

2 Background

Registration status

2.1 **TGA status at the time of PBAC consideration:** The submission was made under the TGA/PBAC Parallel Process. At the time of PBAC consideration Spikevax LP.8.1 remained under TGA evaluation. Spikevax was granted full registration on 21 April 2023, with follow-on full registrations for BA.4-5 on 14 August 2023, XBB.1.5 on 6 October 2023 and JN.1 on 14 November 2024. The sponsor advised that it was waiting to receive the final outcome letter relating to Spikevax LP.8.1 from the TGA. The sponsor did not provide any further TGA documentation for Spikevax LP.8.1.

2.2 The TGA approval process for COVID-19 vaccines was established to balance the clinical urgency for COVID-19 vaccines with scientific rigour. For adapted vaccines developed to address new variants, the process means that the TGA may approve COVID-19 vaccines based, initially, on immunobridging studies before large-scale real

world effectiveness data become available. These studies compare immunogenicity data (e.g., antibody levels) generated by a vaccine that is adapted to the circulating variant to a previously approved version of the vaccine. This approach is considered useful when traditional efficacy trials are impractical, such as for variant-specific boosters or paediatric approvals. Sponsors are however required to continue to review follow up clinical studies for safety analyses and submit updates to the TGA for patient information and drug safety as required (paragraph 2.5, raxtozinameran, Public Summary Document [PSD], May 2025 PBAC Meeting).

2.3 Table 2 summarises the TGA registration status of Spikevax COVID-19 vaccine products and related indications. The submission stated that the sponsor has updated the variants of mRNA-1273 to cover XBB.1.5, JN.1 and KP.2, of which XBB.1.5 and JN.1 are TGA-approved. Correspondence received from the sponsor on 6 January 2026 stated that TGA registration was not sought for the KP.2 vaccine, although it was registered for use in a small number of other countries. The correspondence noted that immunogenicity and RWE data are available for the KP.2 vaccine, and these were provided in the submission as they were considered relevant for an assessment of the mRNA platform.

2.4 The ESC noted the importance of using vaccines that target currently circulating variants, and that vaccines based on earlier viral strains have limited relevance in Australian clinical practice due to reduced effectiveness against predominant SARS-CoV-2 variants.

2.5 The pre-PBAC response stated the platform approach proposed for COVID-19 vaccines is similar to that applied for influenza vaccines, insofar as the request being sought for Spikevax would cover future variant updated vaccines in a similar manner to the current influenza vaccines whereby strains are updated on an annual basis. The response stated that vaccine effectiveness (VE) of updated variant vaccines is expected to be maintained or potentially improved through better antigenic matching to circulating variants. The submission assumed that updated variant vaccines would be available in Australia, however the PBAC considered this would be dependent upon TGA approval, noting that TGA evaluation of Spikevax LP.8.1 was ongoing. The PBAC considered that if Spikevax LP.8.1 is not approved by the TGA, it will have implications for the clinical evaluation of Spikevax, noting that Comirnaty LP.8.1 was granted TGA approval on 1 October 2025[1].

[1] Australian Register of Therapeutic Goods (ARTG) record for COMIRNATY LP.8.1, https://www.tga.gov.au/resources/artg/506526

Table 2: Status of TGA Applications for registration of Spikevax COVID-19 vaccine as reported in submission

Vaccine Name	Application	Formulation	Full/provisional registration date	Indication
SPIKEVAX (elasomeran)	individuals 6 years of age and older	0.2 mg/mL suspension for injection vial	21 April 2023	Active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 6 years of age and older
	individuals 6 years of age and older	0.1 mg/mL suspension for injection pre-filled syringe	21 April 2023	
	individuals aged 6 months to less than 6 years	0.1 mg/mL suspension for injection vial	2 May 2025	
SPIKEVAX Bivalent Original/ Omicron BA.4-5 (elasomeran/ davesomeran)	individuals 12 years and older who have previously received at least a primary vaccination course against COVID-19	0.1 mg/mL suspension for injection – single-dose	8 June 2023	A booster dose for active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 12 years and older who have previously received at least a primary vaccination course against COVID-19
		0.1 mg/mL suspension for injection vial	Provisional 20 February 2023	
		0.1 mg/mL suspension for injection pre-filled syringe	20 February 2023	
SPIKEVAX XBB.1.5 (andusomeran)	individuals 12 years of age and older	0.1 mg/mL suspension for injection pre-filled syringe	10 October 2023	Active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 12 years of age and older
		0.1 mg/mL suspension for injection vial - single-dose	10 October 2023	
SPIKEVAX JN.1 (SARS-CoV-2 JN.1 mRNA)	individuals 12 years of age and older	0.1 mg/mL suspension for injection pre-filled syringe	15 November 2024	As above
SPIKEVAX LP.8.1 (SARS-CoV-2 LP.8.1 mRNA)[a]	individuals 12 years of age and older	0.1 mg/mL suspension for injection pre-filled syringe	TGA evaluation was ongoing at time of PBAC consideration	No TGA documents were provided with the submission for the LP.8.1 vaccine. Draft Product Information was provided after submission.

Source: Adapted from Table 1-17, p44 of the submission.
COVID-19 = coronavirus disease 2019; mRNA = messenger ribonucleic acid; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; TGA = Therapeutic Goods Administration
[a] SPIKEVAX LP.8.1 has been lodged for consideration by the TGA.

2.6 The submission requested NIP listing of mRNA-1273 (Spikevax) updated to target circulating and emerging variants of SARS-CoV-2. As such, the proposed listing is not limited to the current TGA-approved version of Spikevax (JN.1), nor the version of Spikevax under consideration by the TGA currently (LP.8.1). A platform approach would mean that PBAC advice could apply to future adaptations of the mRNA-1273 (Spikevax) vaccine, which would be manufactured by Moderna using the same platform as used for previous Spikevax formulations that have been approved by the

TGA and supplied in Australia through the National COVID-19 Vaccine Program (NCVP). A positive PBAC recommendation for mRNA-1273 (Spikevax) vaccines would not apply to mRNA-1283 (mNEXSPIKE) vaccines, as these are different vaccine products.

Previous PBAC consideration

2.7 This is the first submission for consideration by the PBAC to list Spikevax on the NIP. However, a submission requesting to list Comirnaty (Pfizer Australia Pty Ltd) on the NIP was considered at the May 2025 PBAC meeting and December 2025 Intracycle meeting[2].

ATAGI advice

2.8 The ATAGI provided pre-submission advice to the PBAC dated 20 June 2024. Some key advice is provided below.

- ATAGI considered both mRNA (Spikevax and Comirnaty) vaccines as equivalent based on its review of the scientific evidence (ATAGI 2024 Advice p 4).
- In regard to myocarditis/pericarditis: Aged-specific data from the TGA showed that for individuals aged 18 – 29 years, the rate of myocarditis was 13.3 cases per 100,000 with Spikevax and 8.3 cases per 100,000 with Comirnaty. The evidence in Australia was supported by a study informed by approximately three million participants who had received two primary doses of either Pfizer or Moderna's vaccine in British Columbia, Canada, between January 2021 and September 2021. The study results indicated a higher risk of myocarditis for Spikevax (35.6 cases per million) compared with Comirnaty (12.6 cases per million; ATAGI 2024 advice p 65). ATAGI concluded that post-marketing data indicated an increased risk of myocarditis and pericarditis associated with mRNA COVID-19 vaccines, especially Spikevax, particularly after the second dose (ATAGI 2024 advice p 56).

2.9 The ATAGI provided pre-submission advice to the PBAC dated 24 October 2025. Some key advice is provided below.

- In regard to the comparison of Spikevax and Comirnaty: Overall, it is likely that the recent variants of Spikevax are at least non-inferior in terms of VE and safety. However, the key uncertainty is VE at longer follow-up, particular for the 6 month–12-month interval, where protection is likely to wane. This has implications for the populations who are recommended for doses every 12 months. Notwithstanding, ATAGI maintained that Spikevax and Comirnaty are equivalent and therefore may be used interchangeably (ATAGI 2025 advice p 65).

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2 https://www.pbs.gov.au/industry/listing/elements/pbac-meetings/agenda/pdf/2025/PBAC-Intracycle-meeting-agenda-DECEMBER-2025.pdf, accessed 6 January 2026.

- In its advice dated 20 June 2024, ATAGI considered both mRNA vaccines for COVID-19 (Spikevax and Comirnaty) as equivalent based on the review of scientific evidence at that time. No new evidence was presented when seeking the additional advice, and no new evidence was identified during the drafting of the ATAGI 2025 advice, that would alter this consideration (ATAGI advice p 66).
- VE of Spikevax appeared to wane over a follow up period of 102 days whereas Comirnaty appeared to be relatively stable [over the same period]. However, the confidence intervals at later follow-up (≥102 days for rRNA-1273; and 84–<112 days for Comirnaty) appear to overlap. Overall, it was unclear whether there is a difference in duration of response across the two vaccines (ATAGI 2025 advice p 63).
- In regard to myocarditis/pericarditis:
    - Overall, a dose of either Spikevax or Comirnaty increases the likelihood of myocarditis compared to no mRNA COVID-19 vaccine. Rates appear slightly higher with Spikevax in males aged 12–17 and 18–29 years, receiving a second dose. Rates in individuals aged ≥60 years appear relatively low (ATAGI 2025 advice p59).
    - Overall, a dose of either Spikevax or Comirnaty increases the likelihood of pericarditis compared to no mRNA COVID-19 vaccine. However, rates appear similar between the two vaccines, with the 18–29 and 30–39 age groups reporting the highest risk. Rates in individuals aged ≥60 appear relatively low. (ATAGI 2025 advice p59).

2.10 The ESC noted ATAGI's advice above (paragraph 2.9) that Spikevax and Comirnaty are equivalent and may be used interchangeably in the proposed NIP populations, which refer to annual or biannual doses. The ESC noted this advice concerning interchangeability does not apply to individuals requiring two or more doses as a primary vaccination series, and that the AIH states it is generally preferable to use the same brand of COVID-19 vaccine for the primary course when multiple doses are recommended (e.g. for people who are severely immunocompromised) although an alternative brand can be used for subsequent doses if necessary (e.g. the brand used for a previous dose is not available).[3] The ESC noted that NIP listing was not requested for primary doses.

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

[3] https://immunisationhandbook.health.gov.au/contents/vaccine-preventable-diseases/covid-19

3 Requested listing

Name (Active ingredient)	Strength	Form	Dosage	Container (Pack Size)	Age(s) of administration(s)	Requested price per dose	Brand Name
Spikevax LP.8.1 (SARS-CoV-2 LP.8.1 mRNA)	0.1 mg/mL	Suspension for injection	Each dose (0.5 mL) contains 50 µg	10 pre-filled syringes	Eligible adults aged 18 years and older	$[redacted][a]	Spikevax®

Source: Table 1-19, p46 of the submission
mg = milligrams, mL = millilitre; µg = micrograms; mRNA = messenger ribonucleic acid; SARS-CoV-2 = severe acute respiratory syndrome coronavirus-2.
[a]Proposed price sourced from page 150 of the submission.

NIP listing: A single injection every 6 or 12 months for vaccination against COVID-19 caused by SARS-CoV-2 in eligible individuals aged 18 years and older			
Age		**Booster dose frequency**	
Adults aged 75 years and older		Recommended every 6 months	
Adults aged 18 to 64 years with severe immunocompromise [a]		Recommended every 12 months	
Adults aged 65 years and older		Recommended every 12 months	
Aboriginal and Torres Strait Islander individuals aged 50-64 years with or without medical risk conditions[b]		Recommended every 12 months	
Disease:	**Vaccine:**	**Program setting**	**Implications for other NIP vaccines**
COVID-19	Single dose mRNA-1273, 0.5 mL (50 µg), intramuscular injection	GPs Local council immunisation clinics Community health centres Aboriginal Medical Services, Pharmacies	None

Source: Table 1-18, p46 of the submission.
COVID-19 = Coronavirus disease 2019; GP = general practitioner; µg = microgram; NIP = National Immunisation Program; mRNA = messenger ribonucleic acid; SARS-CoV-2 = severe acute respiratory syndrome coronavirus-2.
[a]Refer to the Australian Immunisation Handbook for severely immunocompromising conditions for which additional doses of COVID-19 vaccine are recommended
[b]Such as the presence of other medical conditions that may increase the risk of severe COVID-19. Refer to the Australian Immunisation Handbook for specified medical risk conditions that increase the risk of severe COVID-19

3.1 Table 3 summarises the ATAGI recommendations for COVID-19 vaccines as advised in August 2025. The submission requested NIP listing where the ATAGI advice uses the word "recommended" in Table 3. The ESC considered the requested populations were consistent with advice from the ATAGI that emphasised that populations with medical risk conditions are heterogenous, and that ATAGI did not support an overall recommendation for vaccination in groups where its advice was to "consider" a dose based on individual risk-benefit assessment. The ESC noted that where ATAGI's advice used the word "recommended" it indicates that the benefits of vaccination are thought to outweigh the risks for the population described, as set out in Table 3.

Table 3: ATAGI COVID-19 Vaccine Recommendations

Age group	ATAGI Recommendation	Requested NIP Listing
No Medical Risk Conditions		
6 months to <5 years	Not recommended	None
5 years to <18 years		
18–64 years	Consider 1 dose each year	None
65–74 years	Recommend 1 dose each year	Eligible for 1 dose each year
≥75 years	Recommend 2 doses each year	Eligible for 2 doses each year
Medical Risk Conditions[a]		
6 months to <5 years	Consider 1 dose each year	None
5 years to <18 years		
18–64 years		
65–74 years	Recommend 1 dose each year and consider second dose	Eligible for 1 dose each year. Privately purchase 2nd dose if desired.
≥75 years	Recommend 2 doses each year	Eligible for 2 doses each year
Severe Immunocompromise[b]		
6 months to <5 years[b]	Consider 1 dose each year	None
5 years to <18 years		
18–64 years	Recommend 1 dose each year and consider second dose	Eligible for 1 dose each year. Privately purchase 2nd dose if desired.
65–74 years		
≥75 years	Recommend 2 doses each year	Eligible for 2 doses each year
Aboriginal and Torres Strait Islander people aged 50 to 74 years		
No Medical Risk Conditions	Recommend 1 dose each year	Eligible for 1 dose each year
With Medical Risk Conditions	Recommend 1 dose each year and consider second dose	Eligible for 1 dose each year. Privately purchase 2nd dose if desired.
Pregnant People[c]		
Consider a dose in the second or third trimester from 20 weeks of gestation in each pregnancy		None

Source: Table of ATAGI recommendations for Covid-19 vaccines (October 2025 pre-submission Advice), Attachment A accompanying the submission.

ATAGI = Australian Technical Advisory Group on Immunisation; NIP = National Immunisation Program

[a]As specified the Australian Immunisation Handbook COVID-19 Chapter.

[b]Children aged 6m to <5y with severe immunocompromise receiving COVID-19 vaccine for the first time or people being revaccinated after haematopoietic stem cell transplant (HSCT) or CAR-T cell therapy should receive 2 'priming' doses, 8 weeks apart.

[c]ATAGI recommendations updated in May 2025 note the following: pregnant women who have previously been vaccinated are not routinely recommended to have a further dose of COVID-19 vaccine. However, they can consider a further dose of COVID-19 vaccine based on presence of underlying risk conditions and/or personal preference.

Previously vaccinated pregnant women who have no conditions that increase the risk of severe illness from COVID-19 have a very low risk of severe illness and pregnancy complications from Omicron infection. However, a dose administered during pregnancy may reduce the risk of COVID-19 infection and hospitalisation in young infants through transplacental passage of antibodies, noting that the risk of severe illness in healthy young infants is extremely low (Australian Immunisation Handbook, updated May 2025).

The Australian Immunisation Handbook includes examples of conditions associated with increased risk of severe outcomes from COVID-19 and examples of severely immunocompromising conditions for which additional doses of COVID-19 vaccine are recommended or can be considered.

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

4 Population and disease

4.1 COVID-19 is an infectious disease caused by SARS-CoV-2, an enveloped positive-sense single-stranded genomic RNA virus belonging to the Coronaviridae family of viruses. It was first reported in December 2019 in Wuhan, China, and soon after, the virus and the disease spread across the globe.

4.2 The primary mode of transmission of SARS-CoV-2 is person to person via respiratory droplets which infect mucosal surfaces (e.g., nose, mouth and eyes). The severity of COVID-19 ranges from asymptomatic to critical illness.

4.3 Older individuals ≥60 years old and those with underlying health conditions (e.g., diabetes, cardiac disease, pulmonary disease, immunosuppression) have a greater risk of developing severe or critical disease.

4.4 'Long COVID' (sometimes referred to as 'post-acute sequelae of COVID-19' [PACS] or post-COVID condition) is a condition where patients experience a broad range of persistent or new symptoms following the acute phase of COVID-19 illness. The pathogenesis and prevalence of prolonged symptoms after recovery from acute COVID-19 remain poorly understood. Published estimates range from 6.9% to 15.0% of all COVID-19 cases (para 4.6, raxtozinameran PSD, May 2025 PBAC meeting).

4.5 The World Health Organisation (WHO), the United States (US) Centers for Disease Control and Prevention (CDC), and the European Centre for Disease Prevention and Control (ECDC) have developed tracking systems to characterise SARS-CoV-2 variants that pose a threat to global public health due to increased transmissibility and virulence. Based on regular reviews by WHO, the European Medicines Association (EMA) and the Food and Drug Administration (FDA), the authorities make recommendations for the antigenic composition of future formulations of COVID-19 vaccines to enhance vaccine-induced immune responses to circulating SARS-CoV-2 variants.

4.6 The WHO Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC) regularly assess the implications of SARS-CoV-2 evolution for COVID-19 vaccine antigen composition and advise WHO on whether changes are required to the antigen composition of future COVID-19 vaccines.

4.7 The Australian Institute for Health and Welfare (AIHW) report, Australia's Health 2024, identified COVID-19 as one of the top 5 leading causes of mortality in Australia in 2022. The Australian Respiratory Surveillance Report – 30 December to 26 January 2025 reported that COVID-19 was the leading cause of acute respiratory infection mortality across 2022 – 2024[4].

4.8 The Request for ATAGI pre-submission Advice to the PBAC noted that the JN.1, KP.2, KP.3.1.1, and XEC variants were the strains most likely to cause breakthrough infections amongst previously vaccinated individuals. Of note, NB.1.8.1 (variant under monitoring) is the current dominant SARS-CoV-2 variant (14 July to 10 August 2025) accounting for 72.2% of sequences in Australia[5].

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4 https://www.health.gov.au/sites/default/files/2025-01/australian-respiratory-surveillance-report-30-december-2024-to-26-january-2025.pdf

5 https://www.health.gov.au/sites/default/files/2025-08/australian-respiratory-surveillance-report-28-july-to-10-august-2025.pdf

4.9 The reported incidence of COVID-19 by age group in Australia is presented in Table 4, noting that these numbers are likely to significantly under-report the true incidence of COVID-19, given the current self-testing regime.

Table 4: Incidence of COVID-19[a] in Australia by age group (2020 to 2025)

	Diagnosis year					
Age group (years)	**2020**	**2021**	**2022**	**2023**	**2024**	**2025[a]**
<20	3,928	129,153	2,447,967	121,252	52,588	31,089
20–49	14,888	308,118	5,053,831	349,841	101,473	47,826
50-64	4,709	67,195	1,668,586	173,575	56,063	23,940
65–74	1,827	20,371	622,610	92,573	40,294	18,063
≥ 75	2,799	13,427	485,825	126,515	91,075	42,971
No information	23	349	16,915	635	347	131
TOTAL	28,174	538,613	10,295,734	864,391	341,840	164,020

Source: Table 1-8, p30 of the submission.
COVID-19 = coronavirus disease 2019; NNDSS = National Notifiable (Communicable) Diseases Surveillance System 2025
[a]Confirmed or probable up to 17 June 2025. Note: COVID-19 case notifications in the NNDSS are now a considerable underestimate of the true incidence of COVID-19 in Australia.

4.10 Overall, the total of number of reported cases of COVID-19 are decreasing since the peak in 2022. The submission stated that these numbers are likely an underestimate as collection of self-reported rapid antigen test (RAT) results had ceased in December 2023. The 2025 ATAGI Advice considered this was reasonable; however, this is unlikely to have a significant effect on the estimated disease burden of COVID-19 as the primary goal of vaccination is reduction in hospitalisation/mortality, and these data are likely to be accurately captured.

4.11 According to the National Hospital Morbidity database, risk of hospitalisation due to COVID-19 is directly related to age, with a substantial increase in risk starting from 65 years of age (Table 11, p15 of 2025 ATAGI pre-submission Advice). Compared to patients who contracted influenza or respiratory syncytial virus (RSV), COVID-19 patients tended to be older. The ATAGI advice reported that length of hospital stay was comparable to influenza patients, however, COVID-19 patients tended to have a shorter stay in an intensive care unit (ICU) and were less likely to require mechanical ventilation. In contrast, COVID-19 patients were more likely to die in hospital, of any cause, compared with those admitted with either influenza or RSV.

4.12 The 2025 ATAGI Advice noted that deaths associated with COVID-19 are decreasing, and that deaths tend to peak in line with higher incidence of notified cases (i.e., more serious cases). Mortality due to COVID-19 remains higher than deaths due to influenza, with most deaths occurring in individuals aged over 60 years.

4.13 Spikevax (mRNA-1273) is an mRNA vaccine, a nucleoside-modified mRNA-based vaccine that encodes the SARS-CoV-2 spike protein (S). The role of S is to mediate binding and fusion of the virus to host cell receptors, allowing the virus to enter host cells and replicate. S is a key target of neutralising antibodies (nAB) and therefore an important antigen for vaccine development. Spikevax is formulated in lipid particles,

which enable delivery of the nucleoside-modified mRNA into host cells to allow expression of the SARS-CoV-2 S antigen.

4.14 The evolution of variants of the virus over time has prompted adaptations of the original Spikevax vaccine (and Comirnaty) so that the nucleoside-modified RNA encoding the viral spike protein was adapted to match the prevailing strains of SARS-CoV-2. The rationale surrounding the need to match COVID-19 vaccines to currently circulating variants is to achieve enhanced protection against symptomatic and severe disease, and that vaccines matched to previous variants offer significantly reduced protection against severe COVID-19 outcomes, given the high mutagenicity of SARS-CoV-2.

4.15 The submission noted that the sponsor has developed a rapid-response proprietary vaccine platform based on a mRNA delivery system. The Spikevax mRNA-1273 platform is based on the principle and observations that cells in vivo can take up mRNA, translate it, and then express protein viral antigen(s). The submission proposes addition of mRNA-1273.xxx (Spikevax), to the NIP, where the xxx refers to future variant-adapted vaccines that do not yet have a specific number. Some example mRNA-1273 vaccines include (target variants shown in brackets):

- Bivalent mRNA-1273.214 (ancestral Wuhan-Hu-1 and omicron BA.1)
- Bivalent mRNA-1273.222 (ancestral Wuhan-Hu-1 and omicron BA.4/BA.5)
- Bivalent mRNA-1273.231 vaccine (omicron BA.4/BA.5 and omicron XBB.1.5),
- Monovalent mRNA-1273.815 (XBB.1.5 variant vaccine),
- Monovalent mRNA-1273.167 (JN.1 variant vaccine),
- Monovalent mRNA-1273.712 (KP.2 variant vaccine).

4.16 The submission also stated that the platform approach allows for new variant-containing COVID-19 vaccines to be registered based on its manufacturing/quality (CMC) and nonclinical immunogenicity data, without requiring new human clinical trial data. This process is underpinned by evidence demonstrating clinical safety and immunogenicity of Spikevax.

4.17 Changes in the circulating SARS-CoV-2 variants could result in changes in transmissibility or pathogenicity. Thus, the clinical need for further doses of Spikevax is not static and may change over time. For example, the Omicron variants of SARS-CoV-2 have been associated with lower hospitalisation rates and mortality compared to the Delta variant (independent of previous immunity), which may support limiting availability of COVID-19 vaccines to those at high risk of severe COVID-19 but, if the circulating variant becomes more pathogenic, then the populations for whom the vaccine is recommended may require expansion (paragraph 4.15, raxtozinameran PSD, May 2025 PBAC Meeting).

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

5 Comparator

5.1 The sponsor has nominated the following comparators:

- Main: No vaccination
- Near market: TGA approved mRNA vaccines for the prevention of infection with SARS-CoV-2 updated to the latest variants, specifically, Comirnaty (also known as BNT162b2 [sponsor: Pfizer Australia Pty Ltd]).

5.2 The nominated comparators were reasonable. However, should Comirnaty be listed on the NIP, Comirnaty adapted for the most recent variants would be the appropriate main comparator. The ESC noted that the PBAC recommended Comirnaty for NIP listing in December 2025.

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

6 Consideration of the evidence

Sponsor hearing

6.1 There was no hearing for this item.

Consumer inputs

6.2 The PBAC noted and welcomed the input from two organisations (2) via the Office of Health Technology Assessment Consultation Hub. Both organisations supported the proposed NIP listing of Spikevax, however their comments were not limited to Spikevax in isolation. The input related to the impact of COVID-19 on individuals and the community, and the benefits of effective vaccines more generally.

6.3 The input from the Pharmaceutical Society of Australia expressed it is vital that evidence-based vaccines for preventable diseases are available for all Australians, especially those with specific medical needs.

6.4 The input from the Lung Foundation Australia highlighted additional risks of COVID-19 for Australians living with lung diseases including increased risk of symptom exacerbation, lung function deterioration, hospitalisation and even death. The input noted that post-acute sequelae may develop after acute COVID-19 and discussed key risk factors including recurrent COVID-19 infections and not being vaccinated. The Foundation stated it is vital that COVID-19 vaccinations are freely available, particularly among those most at risk of associated harm such as older adults, pregnant people, and people with an underlying health condition such as a lung disease. High-level results from a survey of 3,352 adults living in Australia, found that the number one barrier to receiving vaccination was out-of-pocket costs, while 90% of respondents agreed that COVID-19 vaccines should remain free for all Australians. The input considered it vital that COVID-19 vaccines are made available under the NIP and there should be no gap in provision when the National COVID-19 Vaccine Program concludes.

Clinical studies

6.5 The submission identified 2 clinical trials and 5 real-world observational studies of recent strain variants of the Spikevax vaccine, however only the observational studies reported effectiveness. The evidence presented in the submission to support the clinical claim for effectiveness was therefore essentially based on retrospective observational real world evidence (RWE). This applies to both comparisons: i) Spikevax adapted for recent strains versus no vaccination, and ii) Spikevax adapted to recent variants versus Comirnaty adapted to recent variants.

6.6 Two studies were identified which provided a direct comparison between Spikevax and Comirnaty: Mok et al. (2025) and Pan et al. (2025) provided a direct comparison of XBB.1.5 variants of Spikevax and Comirnaty. The trial by Mok et al. (2025) was a non-randomised trial to compare the safety and immunogenicity of the Comirnaty and Spikevax monovalent XBB.1.5 COVID-19 vaccines in an elderly population. The trial population was 129 older adults (≥60 years) who were recruited between 2 January and 3 February 2024 and received a dose of either Comirnaty (n=59) or Spikevax (n=70) monovalent XBB.1.5 COVID-19 vaccine. The publication did not describe how patients were assigned to the intervention or comparator. Immunogenicity and safety outcomes were followed up over 1 month. The trial by Pan et al. (2025) was a self-controlled case-series which assessed safety outcomes (N=244,494).

6.7 The relevant vaccine efficacy (VE) outcomes are clinical outcomes. The ATAGI 2025 pre-submission advice noted that prior advice given to the sponsor in 2024 considered that symptomatic COVID-19 cases were not appropriate for estimating VE against severe disease. ATAGI recommended that hospitalisation, intensive care unit (ICU) admissions, and deaths due to COVID-19 should be used. ATAGI also noted that medical attendance was of limited utility in the assessment of this submission.

6.8 The included studies and associated reports are presented in Table 5.

Table 5: Key studies and associated reports of Spikevax (mRNA-1273) and Comirnaty (BNT162b2) presented in the submission

Study ID	Protocol title/ Publication title	Report/publication citation
Spikevax mRNA-1273 (recent strains) vs. no vaccination		
Study P403 NCT06585241 Figueroa (2025)	Subprotocol 01: A Phase 3b/4, Open-label Study to Assess the Immunogenicity of mRNA-1273.167 in Previously Vaccinated Adults Aged ≥18 Years – Subprotocol 01 to Master Protocol mRNA-1273-P403. Database Lock 11 Dec 2024.	9 May 2025
	Subprotocol 02: A Phase 3b/4, Open-label Study to Assess the Immunogenicity of mRNA-1273.712 in Previously Vaccinated Adults Aged ≥18 Years – Subprotocol 02 to Master Protocol mRNA-1273-P403. Database Lock 11 Nov 2024	16 April 2025
	Figueroa AL et al. Immunogenicity of JN.1- and KP.2-Encoding mRNA COVID-19 Vaccines Against JN.1 Subvariants in Adult Participants.	May 6, 2025. medRxiv https://doi.org/10.1101/2025.05.02.25325954 Final article provided with PSCR

Study ID	Protocol title/ Publication title	Report/publication citation
Spikevax mRNA-1273 (recent strains) vs. no vaccination		
Study P205 (Part J) NCT04927065	Protocol mRNA-1273-P205 (Amendment 10).: A Phase 2/3 Study to Evaluate the Immunogenicity and Safety of mRNA Vaccine Boosters for SARS-CoV-2 Variants. Chalkias S et al. Interim Report of the Reactogenicity and Immunogenicity of Severe Acute Respiratory Syndrome Coronavirus 2 XBB–Containing Vaccines	23 Mar 2023 The Journal of Infectious Diseases 2024; 30:e279–86
Hansen (2025). RWE	Hansen CH et al. Effectiveness of the BNT162b2 and mRNA-1273 JN.1-adapted vaccines against COVID-19-associated hospitalisation and death: a Danish, nationwide, register-based, cohort study.	The Lancet Infectious Diseases 2025; 25:1293-1302
Kopel (2024) RWE	Effectiveness of the 2023–2024 Omicron XBB.1.5-containing mRNA COVID-19 Vaccine (mRNA-1273.815) in Preventing COVID-19–related Hospitalizations and Medical Encounters Among Adults in the United States	Open Forum Infect Dis 2024;11 (12): ofae695. doi: 10.1093/ofid/ofae695
Wilson (2025) a RWE	Wilson A et al. Evaluating the Effectiveness of 2024-2025 Seasonal mRNA-1273 Vaccination Against COVID-19-Associated Hospitalizations and Medically Attended COVID-19 among adults aged≥ 18 years in the United States	medRxiv 2025; 2025.03. 27.25324770
Wilson (2025) b RWE	Wilson A et al. Evaluating the Effectiveness of mRNA-1273.815 Against COVID-19 Hospitalization Among Adults Aged≥ 18 Years in the United States	Infectious Diseases and Therapy 2025; 14: 199-216
Zheng [1] RWE	Zheng Z et al. Effectiveness of 2023-2024 mRNA-1273 Xbb.1.5 Vaccine Against Covid-19 Associated Hospitalizations and Medically Attended Covid-19 in the United States	23 May 2025. Available at SSRN (Preprint): https://ssrn.com/abstract=5258507 or http://dx.doi.org/10.2139/ssrn.5258507
Comirnaty studies used to compare with Spikevax - recent strains (Indirect comparison of clinical outcomes)		
Anderson (2025)	Andersen, KM et al. Effectiveness of BNT162b2 XBB.1.5 vaccine in immunocompetent adults using tokenization in two U.S. states.	Vaccine 2025; 52: p126881, https://doi.org/10.1016/j.vaccine.2025.126881
Hansen (2025)	Hansen CH et al. Effectiveness of the BNT162b2 and mRNA-1273 JN.1-adapted vaccines against COVID-19-associated hospitalisation and death: a Danish, nationwide, register-based, cohort study.	The Lancet Infectious Diseases 2025; 25:1293-1302
Appaneal (2025)	Appaneal, HJ et al. Early effectiveness of the BNT162b2 KP.2 vaccine against COVID-19 in the US Veterans Affairs Healthcare System.	Nature Communications 2025; 16, p. 4033, https://doi.org/10.1038/s41467-025-59344-7
Caffery (2024)	Caffrey, AR et al. Effectiveness of BNT162b2 XBB vaccine in the US Veterans Affairs Healthcare System.	Nature Communications 2024; 15: p. 9490, https://doi.org/10.1038/s41467-024-53842-w
Tartof (2024) a	Tartof, SY et al. Effectiveness of BNT162b2 XBB Vaccine Against XBB and JN.1 Sublineages.	Open Forum Infectious Diseases 2024; 11: no. 7, https://doi.org/10.1101/2023.12.24.23300512
Tartof (2024) b	Tartof, SY et al. Estimated Effectiveness of the BNT162b2 XBB Vaccine Against COVID-19	JAMA Intern Med 2024; 184: 932-940

Study ID	Protocol title/ Publication title	Report/publication citation
Spikevax mRNA-1273 (recent strains) vs. no vaccination		
Nguyen (2025)	Nguyen, JL, et al. Effectiveness of the BNT162b2 XBB.1.5-adapted vaccine against COVID-19 hospitalization related to the JN.1 variant in Europe: a test-negative case-control study using the id.DRIVE platform.	EClinicalMedicine 2025; 79: p102995, https://doi.org/10.1016/j.eclinm.2024.102995
Direct comparison between Spikevax and Comirnaty – Immunogenicity and safety		
Mok (2025)	Mok, CKP et al. Comparison of safety and immunogenicity in the elderly after receiving either Comirnaty or Spikevax monovalent XBB1.5 COVID-19 vaccine.	Journal of Infection 2025; 90 (no. 1), p106374, https://doi.org/10.1016/j.jinf.2024.106374
Pan (2025)	Pan, Y et al. Evaluating the safety of XBB.1.5-containing COVID-19 mRNA vaccines using a self-controlled case series study.	Nature Communications 2025. 16 (1), p 6514, https://doi.org/10.1038/s41467-025-61613-4

Source: Sections 2.1-2.2, pp53-60 of the submission and Section 4 of the ATAGI Pre-Submission Advice.
ATAGI = Australian Technical Advisory Group on Immunisation; BNT162b2 = Comirnaty; COVID-19 = coronavirus disease 2019; RWE = Real World Evidence; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

6.9 The key features of the included studies are presented in Table 6.

Table 6: Key features of the RWE studies presented in the submission providing evidence of effectiveness

Study ID	Study design Outcomes	Relevant strain [Age groups assessed]	Study setting Time period N (number of participants)
Spikevax (mRNA-1273) updated for recent strains vs. no vaccination			
Study P403 (Parts1, 2, 3) NCT06585241 Figueroa. (2025)	Clinical trial Phase 3/4 Immunogenicity Safety Risk of bias: low for immunogenicity but high for safety. There was no pre-defined threshold or titre level, as an appropriate measure of protection, identified in the submission, immunogenicity data from these studies were based on short follow-up periods (up to 6 months). Longer-term data are required to assess response.	**NI** JN.1 (Part 1) [≥18 years] [≥65 years] XBB.1.5 (Part 2) [≥18 years] LP.8.1 (Part 3) [≥18 years] [≥65 years] KP.2 (Part 2) [≥18 years]	USA Approximately 12 months JN.1: N=50 KP.2: N=50
Study P205 (Part J) NCT04927065 Chalkias (2024)	Clinical trial Phase 2/3 Immunogenicity Safety Risk of bias: low for immunogenicity but high for safety.	**NI** XBB.1.5 [≥18 years]	United States Approximately 12 months N=50

Study ID	Study design Outcomes	Relevant strain [Age groups assessed]	Study setting Time period N (number of participants)
Hansen (2025)	RWE Retrospective cohort Mortality Hospitalisation Risk of selection bias and confounding	**NI** JN.1 [≥65 years]	Denmark 1 October 2024 to 31 January 2025 N=894,560
Kopel (2024)	RWE Retrospective cohort Hospitalisation Medical attendance High risk of selection bias and confounding. Medical attendance has limited utility.	**NI** XBB.1.5 [≥18 years] [≥65 years]	United States 12 September 2023 to 15 December 2023 N=859,335 matched pairs
Wilson (2025)	RWE Retrospective cohort Hospitalisation Medical attendance Moderate or high risk of selection bias and confounding. Medical attendance has limited utility.	**Immunocompromised (Hospitalisation)** XBB.1.5 [≥18 years] [≥65 years]	United States 12 September 2023 to 31 December 2023 N=903,349 matched pairs
Wilson (2025)		**NI** KP.2 [≥18 years] [≥65 years]	United States 23 August 2024 to 24 December 2024 N=465,073 matched pairs
Zheng (2025)	RWE Retrospective cohort Hospitalisation Medical attendance Moderate to high risk of selection bias and confounding. Medical attendance has limited utility.	**Immunocompromised** XBB.1.5 [≥18 years] [≥65 years]	United States 1 September 2022 to 21 February 2024 N=903,349 matched pairs
Comirnaty studies used to compare with Spikevax - recent strains (Indirect comparison of clinical outcomes)			
Anderson (2025)	RWE Retrospective cohort Hospitalisation High risk of selection bias and confounding.	**NI** XBB.1.5 [≥18 years]	United States 25 September 2023 to 31 March 2024 N=6,344,448
Hansen (2025)	RWE Retrospective cohort Mortality/Hospitalisation High risk of selection bias and confounding.	**NI** JN.1 [≥65 years]	Denmark 1 October 2024 to 31 January 2025 N=894,560

Study ID	Study design Outcomes	Relevant strain [Age groups assessed]	Study setting Time period N (number of participants)
Appaneal (2025)	RWE Case-control Hospitalisation Medical attendance High risk of selection bias and confounding. Medical attendance has limited utility.	**Immunocompromised** = 40.9% JN.1/KP.2 [≥18 years]	United States 5 September 2024 to 30 November 2024 N=44,598 ARI episodes
Caffery (2024)	RWE Case-control Hospitalisation Medical attendance High risk of selection bias and confounding. Medical attendance has limited utility.	**Immunocompromised** = 35.6% XBB.1.5 [≥18 years]	United States 25 September 2023 to 31 January 2024 N=113,147 ARI episodes
Tartof (2024)	RWE Case-control Hospitalisation Medical attendance High risk of selection bias and confounding. Medical attendance has limited utility.	**Immunocompromised** not reported XBB.1.5 [≥18 years]	United States 10 October 2023 to 10 December 2023 N=8,199 ARI (16.4% (2,977) hospitalised)
Tartof (2024)			United States 10 October 2023 to 29 February 2023 N=52,036 ARI (16.8% (8,732) hospitalised)
Nguyen (2025)	RWE Case-control Hospitalisation High risk of selection bias and confounding.	**Immunocompromised** 2.4 to 7.4% (across vaccinated and non-vaccinated cohorts) XBB.1.5 [≥18 years]	Belgium Denmark, Italy, Navarra (Spain), The Netherlands, Norway, Portugal. N=1425 (21.6% [308] test positive cases)
Direct comparison between Spikevax and Comirnaty			
Mok (2025)	Clinical trial Immunogenicity Safety Low risk of bias for immunogenicity and high risk of bias for safety ((knowledge of allocation) but not informative for vaccine effectiveness.	**Immunocompromised** XBB.1.5 [≥60 years]	Chinese University of Hong Kong Medical Centre or Prince of Wales Hospital in Hong Kong 2 January 2024 to 3 February 2024. N=70
Pan (2025)	Retrospective observational self-controlled case series Safety Non-randomised. High risk of bias for safety (knowledge of allocation).	**Immunocompromised** not reported XBB.1.5 [≥18 years]	United states 11 September 2023 to June 1, 2024 N=244,494

Source: Sections 2.1-2.4, pp53-75 of the submission, Section 4 of the ATAGI Pre-Submission Advice, and main publications of the included studies.

ARI = acute respiratory infections; COVID-19 = coronavirus disease 2019; NI = non-immunocompromised (immunocompetent); RWE = Real World Evidence; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2

[a]Gilbert PB et al. Immune correlates analysis of the mRNA-1273 COVID-19 vaccine efficacy clinical trial. Science 2022; 375:43–50.

[b]Khoury DS et al. Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection. Nat Med 2021; 27:1205–11.

6.10 Two direct trials of Spikevax versus no vaccination were included in the submission as 'pivotal evidence'. However, these trials only assessed short-term immunogenicity and safety with analyses based on small sample sizes. These studies did not assess effectiveness outcomes such as hospitalisations or intensive care admissions, or mortality.

- Study P403 (Figueroa [2025]) had three parts based on type of variant (Part 1: JN.1; Part 2: XBB.1.5 and KP.2; Part 3: LP.8.1).
- Study P205 (Chalkias (2024) (Part J: XBB.1.5).

6.11 The observational and non-randomised studies are inherently subject to a high risk of selection bias and confounding, although attempts were made to mitigate confounding in some of the studies. Furthermore, different durations of follow-up and differences in circulating variants made it difficult to conduct cross-study comparisons. The evaluation stated it was unclear whether there were differences between variants of concern or variants under monitoring.

Immunogenicity

6.12 Overall, nAb titre levels rose considerably against each of the strains assayed. However, as noted in the 2025 ATAGI Pre-Submission Advice noted , the sponsor has not pre-defined a threshold or titre level as an appropriate measure of protection or immunogenicity. The submission acknowledged that a definitive protective threshold for nAb titres has not been established, making it challenging to define minimal clinically important differences (MCIDs) in immunogenicity outcomes.

6.13 LP.8.1 variant: The submission noted that immunogenicity data from Study P403 Part 3 will be provided by the sponsor once available.

6.14 JN.1 variant: At 29 days of follow up, participants who received the Spikevax reported substantial immunogenic responses, in terms of geometric mean titre (GMT) and geometric mean fold-rise (GMFR) across all SARS-CoV-2 pseudovirus strains, with the strongest responses against JN.1. Seroresponse rate (SRR) ranged from 81.3% against the JN.1 strain to 70.8% against the KP.2 strain.

6.15 KP.2 variant: At 29 days of follow up, participants who received Spikevax (KP.2 variant adapted) reported substantial immunogenic responses. SRR ranged from 81.6% against the XEC strain to 71.4% against the KP.2 strain.

6.16 XBB.1.5 variant: At 29 days of follow up, participants who received Spikevax (XBB.1.5 variant adapted) reported substantial immunogenic responses across all SARS-CoV-2 pseudovirus strains. It was noted in the submission that total response was lowest against the JN.1 strain in terms of GMT.

6.17 The Pre-Sub-Committee Response (PSCR) stated that the sponsor had provided clarification to ATAGI regarding the titre threshold at which clinical protection is

maintained, and provided a copy of the sponsor's response to ATAGI as Attachment 1 to the PSCR. However, the ESC noted that neither the PSCR, nor the provided attachment adequately addressed the concern raised in the evaluation. The situation remained that no pre-defined threshold or titre level, has been defined as an appropriate measure of protection. The PSCR did not provided an adequate discussion of how the immunogenicity data can inform estimation of clinical benefit in terms of mortality and COVID-19 related hospitalisation versus no vaccine or versus Comirnaty. As such, the ESC agreed with the evaluation that the interpretation of immunogenicity data was limited by lack of established thresholds.

Comparative effectiveness

6.18 The evaluation focussed on results of studies that presented an estimate of VE in terms of hospitalisations, intensive care admissions or death. 'Medical Attendance' was also assessed in the included studies. As noted in the 2025 ATAGI Pre-Submission Advice, the outcome of Medical Attendance has limited utility regarding the current assessment of the effectiveness of Spikevax. The ESC agreed with the ATAGI that 'Medical Attendance' was a less relevant outcome compared with hospitalisation and mortality.

6.19 Effectiveness results are presented by outcome, vaccine adapted variant, and by age group where available.

Spikevax versus no vaccination

Mortality

6.20 JN.1 variant: A single study of Spikevax (JN.1 variant) reported VE against COVID-19-related mortality (Table 7).

Table 7: Summary of vaccine effectiveness of Spikevax (JN.1 variant) to prevent COVID-19 related mortality

Study	Population	COVID-19 strain	Timepoint	VE (95% CI)
Age ≥65 years				
Hansen (2025)	JN.1 vaccinated= 91,461 No JN.1 vaccination= 859,216	Any lineage (2024–2025)	Mean=100.4 days	95.8% (69.2; 99.4)[a]

Source: Table 2-25, p93 of the submission

CI= confidence interval; COVID-19= coronavirus disease 2019; VE= vaccine effectiveness.

[a]Except where otherwise indicated, model adjustment was for age, sex, geographical region, comorbidities (none, one, two, three or more), number of previous COVID-19 booster vaccines, migration heritage, whether previously hospitalised for COVID-19, and whether previously tested positive for SARS-CoV-2. Adjustment variables restricted to age, comorbidities (none, one, two, three or more), number of previous COVID-19 booster vaccines, and whether previously hospitalised for COVID-19

6.21 In individuals aged ≥65 years who were vaccinated with Spikevax versus those who were not, Spikevax was associated with a VE against mortality of 95.5%.

6.22 KP.2, XBB.1.5, and LP.8.1 variants: There were no studies of Spikevax that reported on VE against COVID-19-related mortality for these variants.

COVID-19-related hospitalisations

6.23 JN.1 variant: Results are presented in Table 8.

Table 8: Summary of vaccine effectiveness Spikevax (JN.1) to prevent COVID-19 related hospitalisation

Study	Population	COVID-19 strain	Timepoint	VE (95%CI)
≥65 years				
Hansen (2025)	JN.1 vaccinated= 91,461 No JN.1 vaccination= 859,216	Any lineage	Mean= 100.4 days	84.9% (70.9; 92.2)[a]

Source: Table 2-25, p93 of the submission

CI= confidence interval; COVID-19= coronavirus disease 2019; HR= hazard ratio; VE= vaccine effectiveness

[a]Adjusted ratios were calculated for the weighted sample using a weighted Cox regression model that included mRNA-1273 KP.2 vaccination status and any covariates with a standardised mean difference greater than 0.1 after inverse probability of treatment weighting.

6.24 In individuals aged ≥65 years who were vaccinated with Spikevax versus those who were not, Spikevax was associated with a VE against hospitalisation of 84.9% at a median follow-up of 100.4 days.

6.25 KP.2 variant: Results are presented in Table 9.

Table 9: Summary of vaccine effectiveness of Spikevax (KP.2 variant) to prevent COVID-19 related hospitalisation

Study	Population	COVID-19 strain	Timepoint	VE (95%CI)
≥18 years				
Wilson (2025)	KP.2 vaccinated= 465,073 No 2024-2025 vaccination= 465,073	Any lineage	Median: 57 days IQR= 32–77 days	52.8% (34.8; 65.8)[a]
≥65 years				
Wilson (2025)	KP.2 vaccinated= 258,098 No 2024-2025 vaccination= 258,098	Any lineage	Median: 57 days IQR= 32–77 days	53.2% (34.2; 66.7)[a]

Source: Table 4-9 of ATAGI Pre-Sub mRNA-1273 final

CI= confidence interval; COVID-19= coronavirus disease 2019; VE= vaccine effectiveness.

[a]Adjusted ratios were calculated for the weighted sample using a weighted Cox regression model that included mRNA-1273 KP.2 vaccination status and any covariates with a standardised mean difference greater than 0.1 after inverse probability of treatment weighting.

6.26 In individuals aged ≥65 years who were vaccinated with Spikevax versus those who were not vaccinated, Spikevax was associated with a VE against hospitalisation of 52.8% at a median follow-up of 57 days. A similar VE (53.2%) was reported for all adults aged ≥18 years.

6.27 An extended final analysis of Wilson (2025) (Vicic [2025] in press)[6] over a median follow-up of 127 days reported that VE was 47.1% (95% CI: 39.3%, 53.8%) in adults over the age of 65 years compared with 53.2% (34.2%, 66.7%) at interim analysis (the intake period ended 24 December 2024, and patients were followed through 31 December 2024). The final publication by Vicic et al. (2026) was provided with the PSCR[7].

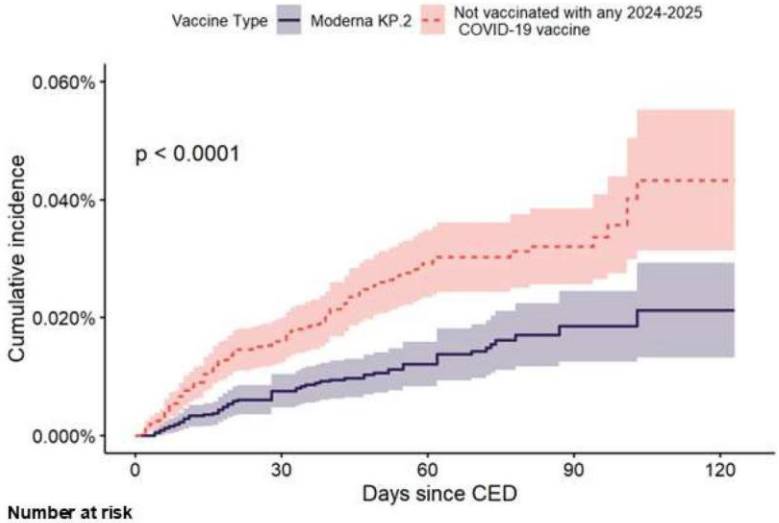
6.28 The 2025 ATAGI Pre-Submission Advice noted that long-term data (up to 120 days follow-up) on the cumulative incidence of COVID-19 hospitalisations for the KP.2 variant were also provided by the sponsor from the observational study by Wilson et

[6] Vicic N et al (2025, In Press). Evaluating the Effectiveness of 2024-2025 Seasonal mRNA-1273 Vaccination Against COVID-19-Related Hospitalizations and Medically Attended COVID-19 among adults aged ≥ 18 years in the United States.

[7] Vicic N, et al. Evaluating the Effectiveness of 2024-2025 Seasonal mRNA-1273 Vaccination Against COVID-19-Related Hospitalizations and Medically Attended COVID-19 Among Adults Aged ≥ 18 years in the United States: An Observational Matched Cohort Study. Infect Dis Ther. 2026 Jan 10. doi: 10.1007/s40121-025-01292-2.

al. (2025a and 2025b()[8,9] as shown in Figure 1. This study of mRNA-1273 (Spikevax) targeting the KP.2 SARS-CoV2 variant was used to inform the economic model (Wilson et al. (2025b).

Figure 1: Cumulative incidence of COVID-19 hospitalisations

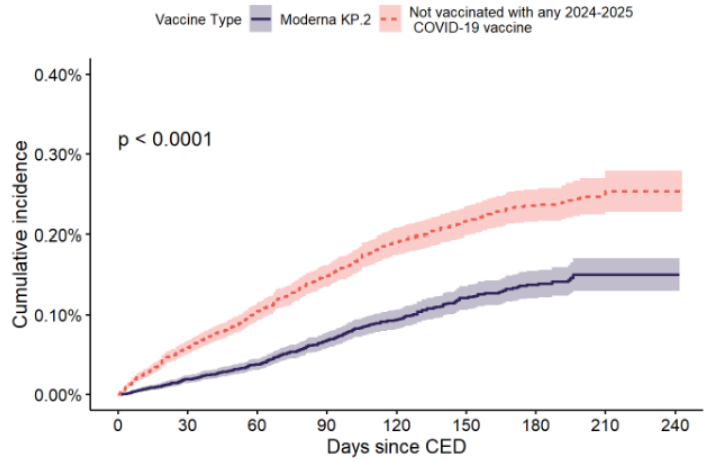


Source: Figure 6, p48 of the ATAGI pre-submission Advice 2025. (Source for ATAGI Advice: Figure 3, Wilson et al. [2025])
CED= Cohort entry date; COVID-19= coronavirus disease 2019

6.29 Longer follow-up data (up to 240 days follow-up) from Wilson (2025) have also become available (Vicic et al [2025], In Press) are depicted in Figure 2.

[8] Wilson, A et al. Evaluating the Effectiveness of mRNA-1273.815 Against COVID-19 Hospitalization Among Adults Aged >/= 18 Years in the United States. *Infect Dis Ther* 2025; 14: pp 199-216.
[9] Wilson, A, et al. Evaluating the Effectiveness of 2024-2025 Seasonal mRNA-1273 Vaccination Against COVID-19-Associated Hospitalizations and Medically Attended COVID-19 among adults aged ≥ 18 years in the United States, 2025. 10.1101/2025.03.27.25324770

Figure 2: Cumulative incidence curves of time to COVID-19 -Related Hospitalizations, individuals aged ≥65 years



Source: Figure 6, p48 of the ATAGI pre-submission Advice 2025. Source for ATAGI Advice: Vicic et al (2025):
CED= Cohort entry date; COVID-19= coronavirus disease 2019

6.30 The ATAGI Advice noted that whilst a statistically significant difference was maintained up to 240 days of follow-up, an interval analysis for longer periods of follow-up was required from the sponsor as these data would be more informative at estimating longer-term VE. These data were most relevant to populations where vaccination is every 12-months.

6.31 XBB.1.5 variant: Three studies of Spikevax (XBB.1.5 variant) reported on VE against COVID-19-related hospitalisation in individuals aged ≥18 years and in individuals aged ≥65 years. Data were also provided for immunocompromised individuals (Table 10).

Table 10: Summary of vaccine effectiveness of Spikevax (XBB.1.5) to prevent COVID-19 related hospitalisation

Study	Population	COVID-19 strain	Timepoint	VE (95%CI)
Age ≥18 years				
Kopel (2024)	XBB.1.5 vaccinated=859,335 No 2023-2024 vaccination=859,335	Any lineage	Median= 63 days IQR= 44-78 days	60.2% (53.4; 66.0)
Wilson (2025)	XBB.1.5 vaccinated= 1,272,161 No 2023-2024 vaccination= 1,272,161	Any lineage	Median= 84 days IQR= 58–101 days	51% (48; 54)[a]
Zheng (2025)	XBB.1.5 vaccinated= 903,349 No XBB.1.5 vaccination= 903,349	Any lineage (JN.1 predominant)	Median= 111 IQR= 81–128 days	56% (52; 60)
			8-30 days	67% (60; 73)
			8-120 days	57% (52; 61)
Age ≥65 years				
Kopel (2024)	XBB.1.5 vaccinated=465,061 No 2023-2024 vaccination=465,061	Any lineage	Not stated	60.5% (53.3; 66.6)
Wilson (2025)	XBB.1.5 vaccinated= 294,388 No 2023-2024 vaccination= 294,388	Any lineage	Median= 84 days IQR= 58–101 days	56% (51; 61)[a]
Zheng (2025)	XBB.1.5 vaccinated= 681,891 No XBB.1.5 vaccination= 681,040	Any lineage (JN.1 predominant)	Median= 111 IQR= 81–128	58% (54; 62)
Immunocompromised (Not grouped by age)				
Wilson (2025)	XBB.1.5 vaccinated= 236,490 No 2023-2024 vaccination= 147,522	Any lineage	Median= 84 days IQR= 58–101 days	46% (39; 52)[a]
Zheng (2025)	XBB.1.5 vaccinated= 2924 No XBB.1.5 vaccination= 2790	Any lineage (JN.1 predominant)	Median= 111 IQR= 81–128	52% (43; 59)

Source: Table 2-28, p97 of the submission.
CI= confidence interval; COVID-19= coronavirus disease 2019; IQR= inter-quartile rate; SMD = standard mean difference; VE= vaccine effectiveness.
[a]Adjusted ratios were calculated for the weighted sample using a weighted Cox regression model that included Spikevax (mRNA-1273 KP.2) vaccination status and any covariates with an SMD greater than 0.1 after weighting

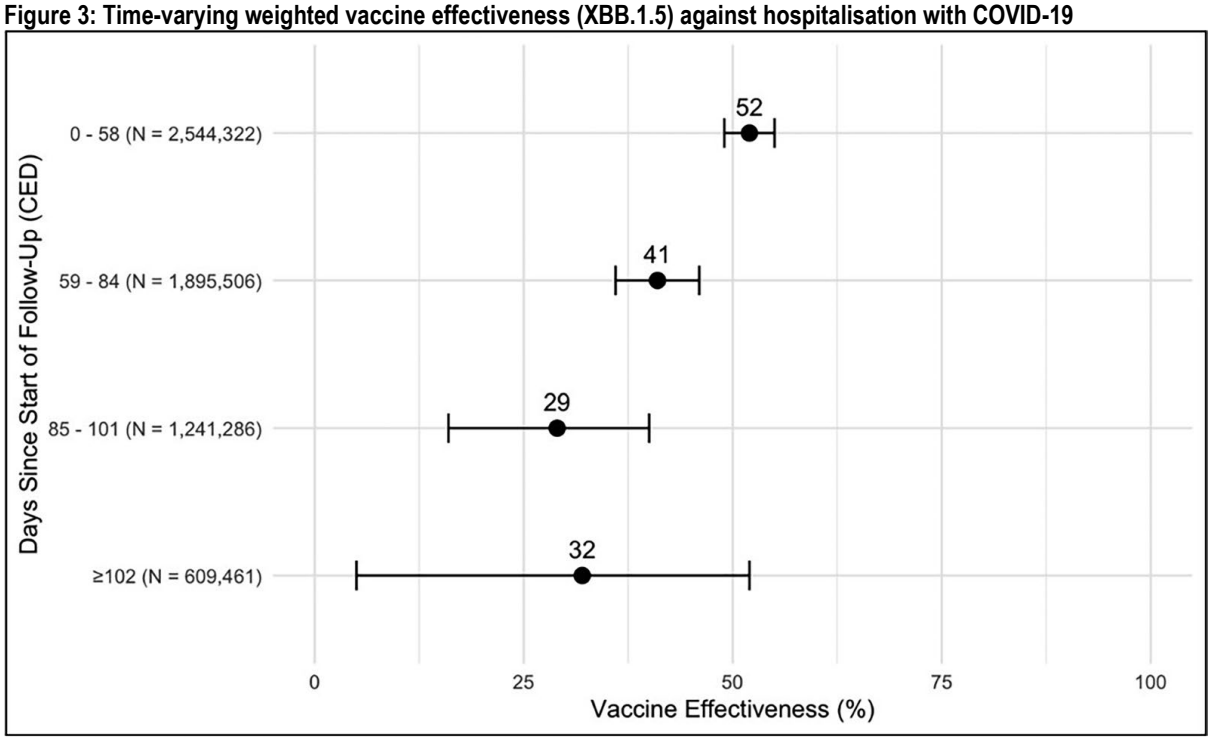
6.32 The included studies indicated that in individuals aged ≥18 years who were vaccinated with Spikevax versus those who were not, Spikevax was associated with a VE against hospitalisation of 56% (95% CI: 52%; 60%) at a median duration of follow-up of 111 days (Zheng [2025]).

6.33 Similarly, in individuals aged ≥65 years who were vaccinated with Spikevax versus those who were not vaccinated, Spikevax was associated with a VE against hospitalisation of 58% (95% CI: 54%; 62%) at a median duration of follow-up of 111 days.

6.34 In immunocompromised individuals who were vaccinated with Spikevax versus those who were not vaccinated, Spikevax was associated with a VE against hospitalisation of 52% (95%CI: 43%; 59%) at a median duration of follow-up of 111 days.

6.35 Interval analysis of hospitalisation (XBB.1.5 variant) to assess waning of VE: The submission presented an interval analysis of hospitalisation from Wilson (2025). This is depicted in Figure 3. The 2025 ATAGI pre-submission Advice also presented tabulated data for the interval analysis (Table 11).

Figure 3: Time-varying weighted vaccine effectiveness (XBB.1.5) against hospitalisation with COVID-19



Source: Figure 2-10, p96 of the submission.
CED = Cohort entry date; COVID-19 = coronavirus disease 2019.
Maximum follow up was 128 days as noted in the 2025 ATAGI Pre-Submission Advice (p50)
Time-varying weighted VE against hospitalization with COVID-19. This plot depicts estimates (black dots) and 95% confidence intervals (black line segments) for VE over time. Each estimate corresponds to the VE within a particular interval of follow-up (start of follow-up through 58 days, 59–84 days, 85–101 days, and > 102 days). Sample sizes (N) reflect the number of patients who remain at risk at the start of the time interval, i.e., whose follow-up has not ended by censoring or the outcome prior to the start of the interval.

Table 11: Interval data for Spikevax (XBB1.5) vaccine effectiveness over time against hospitalisation

Interval	VE% (95% CI)
0-58 days	52% (49; 55)
59-84 days	41% (NR)
85-101 days	29% (NR)
102–128[a] days	32% (5; 52)

Source: Table 44, p63 of the 2025 ATAGI Pre-Submission Advice.
CED = Cohort entry date; CI = confidence interval; VE = vaccine effectiveness.
[a] Wilson (2025) reported this as "≥102 days, however the study stated that the maximum follow up period was 128 days (4 months).

6.36 From the period of 102 to 128 days of follow-up, VE against hospitalisation was 32% (95%CI: 5; 52). The evaluation reported that VE appears to wane over a period of 4 months after which the magnitude of effectiveness remains unclear. From a biological plausibility perspective, given that SARS-CoV-2 is highly mutagenic, immune escape from rapidly mutating variants and waning from infection-induced protection (or prior vaccination) is likely to occur. Interpretation of the interval analysis should consider the following:

- The retrospective design of the cohort study and the inherent high risk of residual confounding and selection bias.

- It is difficult to separate out the timing of the variant predominance from the time since vaccination[10,11]. No analyses were presented in these publications to disentangle these effects.
- A key limitation of the database used for these analyses is that variant-specific data were not available, and the diminishing rate of vaccination during the study period would have made it difficult to assess VE in patients subsequently vaccinated when the JN.1 subvariant was predominant.
- An extended follow-up analysis could suffer from the impact of the emergence of new variants, which could potentially affect VE.
- There are inherent limitations associated with administrative claims data with a high risk of bias due to misclassification of the outcome and exposure in this study. Furthermore, claims data may not capture all hospitalisations or vaccination records, particularly among non-insured individuals (of which there is a high proportion in the United States where much of the RWE was sourced), other under-represented minority groups, or those receiving care outside the insurance setting.

Medical Attendance

6.37 No studies of Spikevax (JN.1 variant) reported on medical attendance. The 2025 ATAGI pre-submission Advice noted that the outcome of Medical Attendance has limited utility regarding the current assessment of the effectiveness of Spikevax. The comparison across studies for Medical Attendance are limited as definitions varied across studies. Medical attendance in Zheng (2025) was defined as any medically attended setting (hospital, ED, outpatient, or physician encounters), whereas Andersen (2025) only included emergency department presentation.

6.38 KP.2 variant: At a median follow-up duration of 57 days, VE against medical attendance[12] was 39.4% in individuals aged ≥18 years who were vaccinated with Spikevax versus those who were not. VE in individuals aged ≥65 years was 46.7%.

6.39 XBB.1.5 variant:

[10] Delaunay, CL et al. Effectiveness of COVID-19 vaccines administered in the 2023 autumnal campaigns in Europe: Results from the VEBIS primary care test-negative design study, September 2023-January 2024, *Vaccine* 2024; 42: pp 3931-3937.

[11] Panagiotakopoulos, L. Use of an additional updated 2023–2024 COVID-19 vaccine dose for adults aged≥ 65 years: recommendations of the advisory committee on immunization practices—United States, 2024. MMWR. *Morbidity and Mortality Weekly Report* 73.

[12] At least one claim with COVID-19 ICD-10 diagnosis code in any position or setting (including hospital admissions as in the primary outcome, as well as emergency department visits, urgent care visits, office visits, telemedicine visits, etc.).

- In individuals aged ≥18 years who were vaccinated with Spikevax versus those who were not vaccinated, Spikevax was associated with a VE of 24% (95% CI: 22%; 25%) at a median follow-up period of 111 days (Zheng [2025][13]).
- In individuals aged ≥65 years who were vaccinated with Spikevax versus those who were not vaccinated, Spikevax was associated with a VE of 25% (95% CI: 23%; 27%) at a median follow-up period of 111 days (Zheng [2025]).,
- In immunocompromised individuals aged ≥18 years who were vaccinated with Spikevax versus those who were not, Spikevax was associated with a VE of 24% (95% CI: 20%; 27%) at a median follow-up period of 111 days (Zheng [2025]).

6.40 A key uncertainty is lack of evidence regarding long-term immunogenicity and effectiveness for Spikevax, which has implications for establishing duration of response, in particular for the 12-month period between booster doses and for the indirect comparison with Comirnaty.

Spikevax versus Comirnaty

Immunogenicity

6.41 Mok (2025; N=129): At 29 days of follow-up, both Spikevax and Comirnaty (XBB.1.5 variants) significantly induced nAb titre levels against both XBB.1.5 and KP.2 viral strains. However, day 29 titre levels were significantly higher in Spikevax compared to Comirnaty. The evaluation reported that the clinical significance of this difference remains unclear. Both vaccines significantly induced nAb titres when compared to a greater panel of viral strains. Both vaccines showed comparable levels of inhibition to recent strains (i.e., JN.1).

Naïve indirect comparisons

6.42 Regarding the evidence presented in the submission, the 2025 ATAGI pre-submission Advice noted that the data did not easily permit comparisons. The ATAGI Advice also noted that ATAGI extracted VE data for mortality and hospitalisation where follow-up times could be sourced from the studies (follow up times were converted into days to aid interpretation of the comparisons).

6.43 Where possible, comparisons were made for studies with the longest duration of follow-up. ATAGI noted that 'these were naïve comparisons and not adjusted for potential confounders such as length of follow up and circulating strains during the study period. Therefore, the conclusions reported are to be interpreted with caution.

Mortality

6.44 JN.1 Variant: A naïve indirect comparison for mortality in individuals aged 65 years and over is provided in Table 12. In individuals aged ≥65 years who were vaccinated with Spikevax versus those who were not, Spikevax was associated with a VE against

[13] Zheng, Z et al. Effectiveness of 2023-2024 Mrna-1273 Xbb. 1.5 Vaccine Against Covid-19 Associated Hospitalizations and Medically Attended Covid-19 in the United States. Available at SSRN 5258507.

mortality of 95.8% (69.2%; 99.4%). This estimate was based on 1 death in the Spikevax cohort of 91,461 vaccinated individuals, compared with 84 deaths in the not vaccinated cohort of 859,216. In comparison, the VE estimate for Comirnaty reported by Hansen (2025) was based on 56 deaths in 728,768 individuals in the Comirnaty cohort.

Table 12: VE against mortality[a] comparison between Spikevax and Comirnaty (JN.1 variant)

Spikevax				Comirnaty			
Study	**Mean follow-up (days)**	**Circulating strains**	**VE % (95%CI)**	**Study**	**Mean follow-up (days)**	**Circulating strains**	**VE% (95%CI)**
≥ 65 years							
Hansen (2025) N vaccinated = 91,461. No. of cases = 1 N not vaccinated = 859,216. No. of cases = 84	100.4 days	Any	95.8 (69.2; 99.4)	Hansen (2025) N vaccinated = 728,768. No. of cases = 56 N not vaccinated = 859,216. No. of cases = 84	86.3 days	Any	76.2 (63.4; 84.5)

Source: Table 40, p60 of the 2025 ATAGI pre-submission Advice.
CI = confidence interval; VE = vaccine effectiveness
Note that all follow up times were converted into days to permit a comparison
[a]Death within 30 days of positive test

6.45 Whilst the point estimate of effectiveness numerically favoured Spikevax over Comirnaty, there was substantial overlap in the 95% confidence intervals.

6.46 KP.2 and XBB.1.5 variants: No comparisons were presented.

VE against hospitalisation

6.47 JN.1 variant: A naïve indirect comparison between Spikevax and Comirnaty for hospitalisation in individuals aged ≥65 years is provided in Table 13.

Table 13: VE (against hospitalisation) comparison of Spikevax and Comirnaty (adapted for JN.1 variant)

Spikevax				Comirnaty			
Study	**Mean follow-up (days)**	**Circulating strains**	**VE (95%CI)**	**Study**	**Mean follow-up (days)**	**Circulating strains**	**VE (95%CI)**
≥ 65 years							
Hansen (2025) N vaccinated = 91, 461. No. of cases = 10 N not vaccinated = 859,216. No. of cases = 278	100.4 days	Any	84.9% (70.9; 92.2)	Hansen (2025) N vaccinated = 728,768. No. of cases = 197 N not vaccinated = 859,216. No. of cases = 278	86.3 days	Any	70.2% (62.0; 76.6)

Source: Table 40, p60 of the 2025 ATAGI Pre-Submission Advice and Hansen (2025)[14]
CI = confidence interval; VE = vaccine effectiveness
Note: Follow up times were converted into days to permit a comparison

6.48 VE numerically favoured Spikevax over Comirnaty (84.9% vs. 70.2%), however, the 95% confidence intervals overlapped. The mean follow-up time was slightly longer for Spikevax in this retrospective cohort study.

6.49 KP.2 variant: A naïve indirect comparison of VE against hospitalisation for Spikevax and Comirnaty (KP.2 variant) in individuals aged ≥18 years and ≥ 65 years is summarised in Table 14.

[14] Hansen, CH et al. Effectiveness of the BNT162b2 and mRNA-1273 JN. 1-adapted vaccines against COVID-19-associated hospitalisation and death: a Danish nationwide register-based cohort study. 2025 Available at SSRN 5227321.

Table 14:VE (against COVID-19 related hospitalisation) comparison of Spikevax and Comirnaty (KP.2 variant)

Spikevax				Comirnaty			
Study	**Mean follow-up (days)**	**Circulating strains**	**VE (95%CI)**	**Study**	**Mean follow-up (days)**	**Circulating strains**	**VE (95%CI)**
≥18 years							
Wilson (2025)[a] N vaccinated = 465, 073. No. of cases = 51 N not vaccinated = 465, 073. No. of cases = 118	57 days	Any	52.8% (34.8; 65.8)	Appaneal (2025)[b]	33 days	Any	68% (42; 82)
≥ 65 years							
Wilson (2025)[b] N vaccinated = 257, 673. N not vaccinated = 258, 556	57 days	Any	53.2% (34.2; 66.7)	Appaneal (2025)	33 days	Any	75% (49; 88)

Source: Table 42, p61 of the 2025 ATAGI pre-submission Advice and Table 1, Wilson (2025).
CI = confidence interval; VE = vaccine effectiveness
Note that all follow up times were converted into days to permit a comparison.
[a]N by vaccinated and non-vaccinated arms was not specified by arm. However, 465,073 mRNA-1273 KP.2 recipients were matched 1:1 in the exposed to the non-vaccinated arm based on age, sex, race, ethnicity, geographic region, week of last healthcare activity before start of intake period, evidence of vaccination with a prior season's vaccine during the pre-index period, and the calendar date of the index date.
[b]Cases by arm could not be identified from the publication.

6.50 Whilst VE numerically favoured Comirnaty over Spikevax, the 95% confidence intervals overlapped. This was observed for participants aged ≥18 years old and for those aged ≥65 years. The follow up time for Spikevax was nearly double that for Comirnaty and so would be affected by waning, raising concerns about comparability of the studies in the indirect comparison.

6.51 XBB.1.5 variant: A naïve indirect comparison of VE (XBB.1.5 variant) against hospitalisation in individuals aged ≥18 years and ≥65 years is summarised in Table 15. There are differences in the included studies and VE estimates in Table 15 compared with those considered by the PBAC when considering Comirnaty in May 2025 (Table 10, Raxtozinameran PSD May 2025). Table 15 below presents results for only a single timepoint for each study, whereas the Comirnaty submission had presented results separately for two time periods: Month 1 to 3 in which XBB.1.5 was predominant; and Month 4 to 6 in which JN.1 predominant.

Table 15: VE (against hospitalisation) comparison of Spikevax and Comirnaty (XBB.1.5 variants)

Spikevax				Comirnaty			
Study	**Timepoint (days)**	**Circulating strains**	**VE (95%CI)**	**Study**	**Timepoint (days)**	**Circulating strains**	**VE (95%CI)**
≥18 years							
Kopel (2024)	63	Any	60.2% (53.4; 66.0)	Tartof (2024)[a]	33	Any	62% (32; 79)
Wilson (2025)	84	Any	51% (48; 54)	Caffrey (2024)	54	Any lineage	43% (34; 51%)
Zheng (2025)	111	JN.1 predominant	56% (52; 60)		54	XBB.1.5	61% (44; 73)
					54	JN.1 co-circulation	46% (32; 58)
					55	JN.1	35% (20; 48)
				Tartof (2024)[b]	58	Any lineage	57% (45; 66)
					59	XBB.1.5	65% (41; 79)
					60	JN.1	54% (33; 69)
				Andersen (2025)	118	Any (JN.1/XBB.1.5 predominant)	36% (18; 50)
≥65 years							
Wilson et al. [2]	84 days	Any lineage	56% (51; 61)	Andersen (2025)	33	Any	47% (28; 61)
Zheng et al. [1]	111 days	Any lineage	58% (54; 62)	Tartof (2024)	33	Any	63% (30; 80)

Source: Table 43, p62 of the 2025 ATAGI Pre-Submission Advice
CI = confidence interval; VE = vaccine effectiveness
Note that all follow up times were converted into days to facilitate comparisons
[a]JAMA Intern Med. 2024;184(8):932–940. doi: 10.1001/jamainternmed.2024.1640
[b]Open Forum Infect Dis (2024); 11(7):ofae370; https://doi.org/10.1093/ofid/ofae370

6.52 VE in preventing hospitalisation appeared similar between Spikevax and Comirnaty. When comparing studies with the longest follow-up, Zheng (2025) reported a VE of 56% (95% CI: 52; 60) for Spikevax at a median follow-up duration of 111 days whereas Andersen (2025) reported a VE of 36% (95% CI: 18; 50) for Comirnaty at a median follow-up duration of 118 days. The follow-up times of the studies for individuals aged ≥65 years were too different to permit a useful comparison. Both studies were conducted at a time when the JN.1 strain was in circulation.

6.53 Interval analysis of hospitalisation (XBB.1.5 variant) to assess waning of VE: Table 16 was reproduced from the 2025 ATAGI pre-submission Advice which summarises a naïve indirect comparison of interval data for VE against hospitalisation between Spikevax (XBB.1.5) and Comirnaty (XBB.1.5).

Table 16: Naïve indirect comparison of interval data between Spikevax and Comirnaty (XBB.1.5 variants) for vaccine effectiveness against hospitalisation

Spikevax: Wilson (2025)		Comirnaty: Nguyen (2025)	
Interval	**VE% (95% CI)**	**Interval**	**VE% (95%CI)**
0-58 days	52% (49; 55)	14–<28 days	52.2% (41.3; 61.1)
		28–<56 days	48.9% (17.9; 68.2)
59-84 days	41%	56–<84 days	56.9% (39.5; 69.2)
85-101 days	29%	84–<112 days	54.6% (50.2; 58.5)
102–128[a] days	32% (5; 52)		
NR		112–<154 days	59.5% (21.4; 79.1)

Source: Table 44, p63 of the 2025 ATAGI Pre-Submission Advice
CI = confidence interval; NR = not reported; VE= VE
[a] Wilson (2025) reported this as "≥102 days", however it is noted that the maximum follow up period was 128 days (4 months).
Note that all follow up times were converted into days to facilitate comparisons

6.54 VE of Spikevax appeared to wane over a follow up period of 102 days whereas Comirnaty appeared to be relatively stable over the same period. However, the 95% confidence intervals at later follow-up (≥102 days for Spikevax; and 84–<112 days for Comirnaty) appear to overlap. The evaluation concluded that overall, it is unclear whether there is a difference in duration of VE in preventing hospitalisation across the two vaccines. Longer-term effectiveness, particularly from 6–12 months remains unclear. The timing of the studies and different follow up periods raise concerns of transitivity with regard to circulating strains.

6.55 The PSCR noted the evaluation's observation that VE of Spikevax appeared to wane over a follow up period of 102 days whereas Comirnaty appeared to be relatively stable over the same period as described above (paragraph 6.54), which was based on the naïve indirect comparison of interval data presented in Table 16. However, the PSCR claimed it was unlikely there would be a difference in the durability of VE, in particular one that would favour Comirnaty over Spikevax. The PSCR noted the comparison was based on a limited evidence base of two studies (Spikevax: Wilson 2025 and Comirnaty: Nguyen 2025). The PSCR suggested that the naïve indirect comparison ignored heterogeneity between the studies including geographic location, residual immunity in the underlying population (from infection or vaccination), and duration of follow-up. The ESC noted that transitivity concerns were discussed in the commentary as shown in paragraph 6.54.

6.56 The PSCR stated that the sponsor had provided clarification to ATAGI regarding the relative durability of Spikevax vs Comirnaty and provided a copy of the sponsor's response to ATAGI as Attachment 1 to the PSCR. The PSCR stated that a study of the KP.2 variant vaccine demonstrated "stable" VE with a median follow-up of 127 days (interquartile range: 84-173 days), however the ESC considered this description was incorrect. The ESC noted that the additional reference (Vicic et al 2026), reported effectiveness of the Spikevax vaccine targeting the KP.2 variant, compared to people who did not receive any 2024–2025 COVID-19 vaccine, in preventing COVID-19-associated hospitalisations during the 2024–2025 season in the United States. The results showed there was waning between the two analysis timepoints for

the study with adjusted[15] overall VE against COVID-19-related hospitalisations reported to be 45.2% at the final analysis (median follow-up of 127 days), compared with 52.8% at the interim analysis (median follow-up of 55 days)[16]. The observation remains that the reported VE of Spikevax KP.2 vaccine was comparable with Comirnaty XBB.1.5 vaccine at an early timepoint but the VE of 45.2% at 127 days indicated waning VE for Spikevax KP.2 vaccine, whereas Comirnaty appeared to be relatively stable over the same period (Table 16). The ESC considered the evidence remains inconclusive, given the limited nature of the comparison.

6.57 The PSCR also referred to the study of Mok et al (2025), described in paragraph 6.41. The PSCR claimed that more stable durability of BNT162b2 (Comirnaty) vs mRNA-1273 (Spikevax) was not supported by the comparative immunogenicity data presented by Mok et al (2025). The ESC noted the conclusions of the study authors that Spikevax induced higher cellular and humoral immune responses than Comirnaty in the elderly [at one-month post-vaccination], but was also associated with a higher incidence of fever. The ESC noted that that study by Mok et al (2025) reported immunogenicity and safety results for a cohort aged 60–91 years at a single point in time after vaccination (one month after vaccination) with either Spikevax or Comirnaty and therefore did not provide data with respect to the waning profile of either vaccine.

6.58 Overall, the ESC agreed with the evaluation that it remained unclear whether there is a difference in duration of response across the two vaccines.

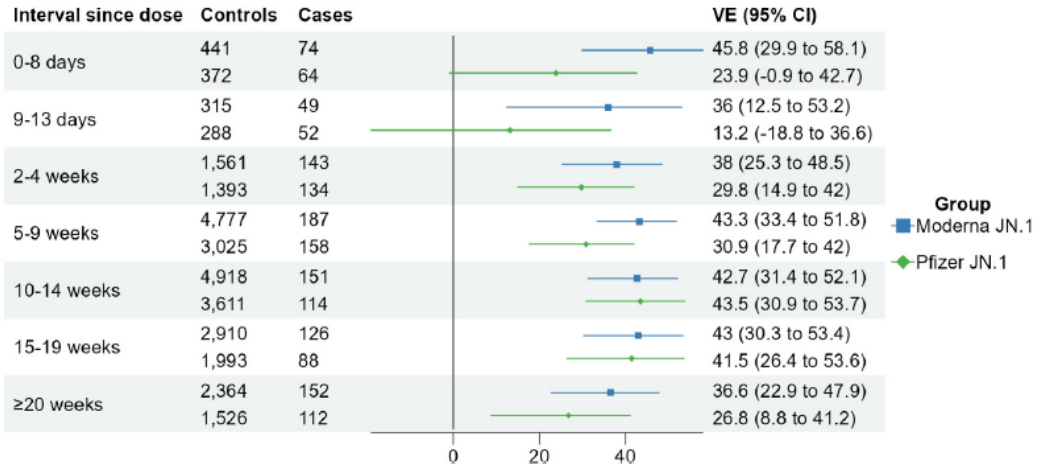
6.59 The pre-PBAC response provided further discussion regarding the comparative effectiveness and durability of Comirnaty vs Spikevax based on a study by Aziz et al (2025)[17]. This was a test-negative case-control study evaluating the effectiveness and waning of Spikevax and Comirnaty against COVID-19 hospitalisation in England using national datasets. VE for Autumn 2024 JN.1 vaccines, including both brands, peaked at 43% (95% CI: 34–51%) at 10–14 weeks and declined to 34% (95% CI: 22–44%) by 20 weeks. The authors noted that lower effectiveness compared with earlier campaigns may reflect high population immunity and heterogeneous circulating lineages. Despite slight differences in point estimates, confidence intervals for both vaccines overlapped at all time points, indicating no significant differences between the VE of the two vaccines (Figure 4).

[15] Adjusted HRs were calculated using a weighted Cox regression model that included mRNA-1273 KP.2 vaccination status and a wide range of baseline covariates.

[16] Final analysis at median follow-up of 127 days (interquartile range 84–173 days); Interim analysis at median follow-up time of 55 days (interquartile range 32–77 days).

[17] Abdul Aziz, N., Kirsebom, F. C. M., Allen, A., & Andrews, N. (2025). Effectiveness of spring 2024 (XBB.1.5) and autumn 2024 (JN.1) COVID-19 vaccination against hospitalisation in England. *Vaccine*, *67*, 127870. https://doi.org/10.1016/j.vaccine.2025.127870

Figure 4: VE of COVID-19 JN.1 vaccines against hospitalisation, stratified by manufacturer (Moderna and Pfizer) and time since vaccination (error bars represent 95 % confidence intervals)



Source: Pre-PBAC response Figure 1, from Aziz et al 2025.

Medical Attendance

6.60 A comparison across studies for medical attendance is problematic as definitions varied across the included studies. For example, Medical Attendance in Zheng (2025) was defined as any medically attended setting which included hospital, Emergency Department [ED], outpatient, or physician encounter settings. On the other hand, Andersen (2025) (publication for Comirnaty) only included emergency department presentations which is deemed more clinically informative. A brief summary of the indirect comparisons is provided below.

6.61 JN.1 variant: No comparison could be made for the JN.1 variants of Spikevax and Comirnaty.

6.62 KP.2 variant: Two studies provided data for a naïve indirect comparison (Wilson [2025] for Spikevax and Appaneal [2025] for Comirnaty). For individuals aged ≥18 years, VE favoured Comirnaty over Spikevax (57.0% [95% CI: 46.0, 65.0] vs. 39.4% [95% CI: 35.0, 43.5]). For individuals aged ≥65 years, VE also numerically favoured Comirnaty over Spikevax (56.0% [95% CI: 44.0, 66.0] vs. 46.7% [95% CI: 41.7, 51.2] vs.). However, there was overlap in the 95% confidence intervals. The follow up time for the Spikevax from the Wilson (2025) study (57 days) was much longer than that for the Comirnaty Appaneal (2025) study (33 days). The evaluation concluded that overall, it was unclear whether there is a difference between vaccines at the same follow up time.

6.63 XBB.1.5: Three studies provided data for Spikevax (Kopel [2025], Wilson [2025, and Zheng [2025]) and three studies (Tartof [2024], Caffery [2024, and Andersen [2025]) provided data for Comirnaty. In individuals aged ≥18 years, Comirnaty appeared more effective than Spikevax in preventing medical attendance. When comparing studies with the longest follow-up, the Spikevax Zheng (2025) study reported a VE of 24% (95% CI: 22, 25) for a median follow-up duration of 111 days. The Comirnaty Andersen (2025) study reported a VE of 45% (95% CI: 34, 54%) for a median follow-up duration

of 118 days. Both studies were conducted at a time when the JN.1 strain was in circulation.

Comparative harms

6.64 Interpretation of the safety data should consider the high risk of bias associated with the open-label design of the included studies.

Spikevax versus no vaccination

6.65 Safety data for unsolicited[18] adverse events (AEs) across the included Spikevax trials have been reproduced from the 2025 ATAGI pre-submission Advice to the PBAC (Table 17).

Table 17: Unsolicited adverse reactions across the Spikevax trials included in the submission (mRNA-1273 - recent strains) stratified by relation to study vaccination

n (%)	Monovalent mRNA-1273.815, 50 µg (N=50)		Monovalent mRNA-1273.167, 50µg (N=50)	Monovalent mRNA-1273.712, 50µg (N=50)
Study **Follow-up period**	**Study P205, Part J** **28 days**	**Study P205, Part J** **181 days**	**Study P403, Part 1** **28 days**	**Study P403, Part 2** **28 days**
Relevant variant	XBB.1.5		JN.1	KP.2
Unsolicited AEs Regardless of Relationship to Study Vaccination				
All	6 (12.0)	24 (48.0)	1 (2.0)	0 (0.0)
Serious	0 (0.0)	2 (4.0)	0 (0.0)	0 (0.0)
Medically-Attended	5 (10.0)	24 (48.0)	1 (2.0%)	0 (0.0)
Severe	0 (0.0)	2 (4.0)	NR	0 (0.0)
Unsolicited AEs Related to Study Vaccination				
All	1 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)
Serious	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Medically-Attended	1 (2.0)	0 (0.0)	NR	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Source: Table 28, pp43-44 of the 2025 ATAGI pre-submission Advice
AEs = adverse reactions. AE = adverse event; mRNA = messenger ribonucleic acid.
mRNA-1273.815 encodes the S protein for Omicron XBB.1.5.
An adverse event was defined as any event that was not present prior to study vaccination or any event already present that worsened in intensity or frequency after vaccination.
NOTES
Medically attended AEs of hypertension and urticaria (both grade 1) in the mRNA-1273 group. Percentages are based on the number of participants in the safety set.
There were no fatal events or events that resulted in study discontinuation.
Results presented as n(%)

6.66 In Study P205, unsolicited TEAEs (up to 28 days) were reported in 6 (12%) participants, of whom five sought medical attention. One of these events was related to the study vaccination. However, no further details were provided in the CSRs. At 6 months of follow-up, approximately half of participants experienced an unsolicited TEAE (not

[18] Solicited adverse events (AEs) in clinical trials are anticipated or common side effects that investigators specifically ask participants about, using structured questions or checklists (like pain, fever, swelling) to assess common reactions to a treatment, especially vaccines. Unsolicited AEs on the other hand are reported spontaneously.

considered related to the study vaccine), all of whom were medically attended. Two participants experienced an AE of special interest (AESI). No other serious adverse events (SAEs), deaths, or AEs leading to study withdrawal were reported across the studies.

6.67 Solicited AEs from Study P205 (Part J) are summarised in Table 18.

Table 18: Solicited and systemic adverse reactions, Spikevax (XBB.1.5 variant) (Study P205, Part J)

Monovalent Spikevax (mRNA-1273.815), 50 µg (N=50)			
Solicited ARs, n(%)		**Systemic ARs, .n(%)**	
Grade 1	23 (46.0)	Grade 1	16 (32.0)
Grade 2	14 (28.0)	Grade 2	12 (24.0)
Grade 3	1 (2.0)	Grade 3	1 (2.0)
Local ARs		**Fever**	
Grade 1	26 (52.0)	Grade 1	1 (2.0)
Grade 2	8 (16.0)	Grade 2	1 (2.0)
Grade 3	0	Grade 3	1 (2.0)
Pain		**Headache**	
Grade 1	28 (56.0)	Grade 1	14 (28.0)
Grade 2	6 (12.0)	Grade 2	3 (6.0)
Erythema (Redness)		**Fatigue**	
Grade 1	1 (2.0)	Grade 1	12 (24.0)
Grade 2	1 (2.0)	Grade 2	10 (20.0)
Swelling (Hardness)		**Myalgia**	
Grade 1	2 (4.0)	Grade 1	14 (28.0)
Grade 2	3 (6.0)	Grade 2	5 (10.0)
Axillary Swelling or Tenderness		**Arthralgia**	
Grade 1	8 (16.0)	Grade 1	12 (24.0)
Grade 2	0	Grade 2	2 (4.0)
		Nausea/Vomiting	
		Grade 1	4 (8.0)
		Chills	
		Grade 1	5 (10.0)
		Grade 2	2 (4.0)

Source: Table 28, p43 of the 2025 ATAGI pre-submission Advice for Spikevax.
AR = adverse reaction

6.68 Study P205 (Part J) was a Phase 2/3 randomised trial comparing the reactogenicity, AEs, and immunogenicity of 50 µg doses of the monovalent mRNA-1273.815 vaccine (50-µg Omicron XBB.1.5 spike protein mRNA) with bivalent mRNA-1273.231 vaccine (25-µg Omicron XBB.1.5 and 25-µg Omicron BA.4/BA.5 spike protein mRNAs). The applicability of this study remains uncertain given that the variants assessed are no longer predominant. The Interim safety data 29 days after vaccination indicated that most local and systemic adverse reactions were mild (Grade 1). There was one serious (Grade 3) systemic AE (fever). Approximately half of all patients reported taking medication to treat pain and/or fever.

6.69 In Study P205 (Part J), the majority of local and systemic AEs were mild (grade 1). There was one serious (Grade 3) systemic adverse reaction (fever). Approximately half of all patients reported taking medication to treat pain and/or fever

6.70 No solicited AEs were provided in the Clinical Study Report (CSR) for Study P403 (Parts 1 and 2). In Study P403 (part 2), no AESIs, SAEs, deaths, or AEs leading to study

withdrawal were reported. There was one serious (Grade 3) systemic adverse reaction (fever) reported in P403 for Spikevax.

6.71 Adverse Events of Special Interest (AESIs):Two AESIs were reported in the P205 (Part J) study for the XBB.1.5 variant. Neither event was deemed related to the study vaccine by the investigator:

- The first participant experienced an event of serious ventricular tachycardia. The patient was discharged 2 days later with medication. As of the end of the study period, the event had not resolved.

6.72 One AESI was reported in the P403 (Part 1) study for the JN.1 variant. One participant who received mRNA-1273.167 presented to the emergency department with chest pain. A small pulmonary embolism was found and treated with anticoagulants. The event was not deemed related to vaccination by the investigator.

Spikevax versus Comirnaty

6.73 The study population in Mok (2025) constituted of 129 individuals ≥60 years of age who were recruited between 2 January and 3 February 2024 and received a dose of either Comirnaty (n=59) or Spikevax (n=70) monovalent XBB.1.5 COVID-19 vaccine.

6.74 AEs were more frequent in the Spikevax arm compared to the Comirnaty arm for both local and systemic reactions. Local reactions included (non-exhaustive) included pain (48.6% vs. 42.4%), pruritus (10.0% vs. 3.4%), and swelling (15.7% vs. 10.2%). Systemic reactions included (non-exhaustive) fever (15.7% vs. 1.7%), fatigue (25.7% vs. 11.9%), muscle pain (12.9% vs. 8.5%), and headache (10.0% vs. 3.4%).

6.75 The majority of reactions were mild and resolved on their own. The authors noted that the higher frequency of adverse events in the Spikevax arm may be associated with a higher dose of mRNA in the vaccine compared to the Comirnaty vaccine (50µg versus 30µg per dose, respectively).

6.76 The ESC noted that a dose of either Spikevax or Comirnaty has been reported to increase the risk of myocarditis or pericarditis compared to no mRNA COVID-19 vaccine, as discussed in paragraph 2.9.

National Centre for Immunisation and Surveillance (2025) systematic review (K=4 studies)

6.77 The 2025 ATAGI pre-submission Advice also presented safety data from the National Centre for Immunisation and Surveillance (2025) systematic review (K=4 studies).

6.78 This review consistently reported that frequency of solicited adverse events was slightly lower in Comirnaty versus Spikevax (Table 19).

Table 19: National Centre for Immunisation and Surveillance (2025) systematic review (K=4 studies): Comparison of solicited adverse events in individuals who received mRNA COVID-19 vaccines

	Spikevax		Comirnaty	
	Dose 1	Dose 2	Dose 1	Dose 2
Local	78%	84.2%	43%	58%
Systemic	74%	88.7%	54.8%	79.5%

Source: Table 37, p58 of the 2025 ATAGI pre-submission Advice.
COVID-19 = against coronavirus disease 2019; mRNA = messenger ribonucleic acid

Benefits/harms

6.79 There was no randomised clinical evidence to support benefit statements for Spikevax. An estimate of benefit and harms is not presented.

Clinical claim

6.80 The therapeutic claims made in the submission were as follows:

- Spikevax (mRNA-1273) is superior in effectiveness and inferior in safety compared to no vaccine in the requested NIP populations.
- Spikevax (mRNA-1273) is at least non-inferior in terms of effectiveness and safety compared to Comirnaty (BNT162b2) in the requested NIP populations.

6.81 The evaluation considered that the therapeutic conclusions presented in the submission are debatable. There were several limitations associated with the observational and retrospective nature of the evidence, and methodological issues regarding estimation of VE in various populations. These limitations engender a high degree of uncertainty regarding the magnitude and the duration of benefit associated with Spikevax vaccination (for most recent circulating variants during conduct of the studies) versus no vaccination. There were similar limitations associated with the evidence for Comirnaty although cautiously, the totality of the evidence presented suggests that Spikevax is likely to be non-inferior to Comirnaty.

6.82 For the comparison between Spikevax (updated variants) versus no vaccination:

- The studies providing evidence of effectiveness were associated with a high risk of section bias and confounding. Notwithstanding the heterogeneity across the studies in terms of study design, patient characteristics, and follow-up durations, there is a high risk of confounding by circulating variants which could impact the magnitude of effectiveness.
- Interval analyses of the Spikevax VE (XBB.1.5 variant) against hospitalisation indicated there was waning of the observed benefit over a period of 4 months after which the magnitude of effectiveness remains unclear. Thus, a key uncertainty is the VE at longer follow-up periods, particular for the 6 month–12-month interval, where protection is likely to further wane. This has major implications for the populations who are recommended for doses every 12 months.

- Most of the evidence presented for Spikevax was based on the JN.1, KP.2, and XBB.1.5 variants. The Spikevax vaccine currently being assessed by the TGA is the Spikevax LP.8.1 (SARS-CoV-2 LP.8.1 mRNA).
- It Is important to consider which estimates of VE will be most relevant for decision-making, i.e., whether it is reasonable to propose a weighted average VE for Spikevax based on earlier time periods in which XBB.1.5 for example was predominant or whether VE of Spikevax now and into the future is most relevant. The evolution of SARS-CoV-2 can be rapid and remains unpredictable. It is likely that vaccines that are better matched to currently circulating variants offer enhanced protection compared with vaccines adapted to respond to previous variants.

6.83 The ESC agreed with the evaluation there were several limitations associated with the observational and retrospective nature of the evidence, along with methodological issues in estimating VE in the requested populations. The ESC also noted considerable heterogeneity across studies (e.g. design, patient characteristics, follow up) making comparisons difficult. In addition, changes in circulating variants during and between studies could influence VE across different timepoints. Other factors impacting effectiveness estimates include uncertainties related to shifts in SARS-CoV-2 transmissibility or pathogenicity, and the unknown performance of future vaccines in the context of ongoing viral evolution, which may or may not allow beneficial cross-reactivity across variants. The ESC also noted that the vaccine's waning profile will affect overall effectiveness in clinical practice, and overall considered there was a high degree of uncertainty regarding the magnitude and the duration of benefit associated with Spikevax vaccination versus no vaccination. Lastly, the ESC noted that updated vaccines lag behind circulating variants, due to the time needed for vaccine development and the TGA evaluation process as a new chemical entity, which contributed additional uncertainty to this assessment.

6.84 Overall, while noting the uncertainties described above (paragraph 6.83), the ESC considered that the submission's claim that Spikevax is superior in effectiveness and inferior in safety compared to no vaccine in the requested NIP populations was supported by the clinical evidence.

6.85 For the comparison between Spikevax versus Comirnaty, the evidence was based on naïve indirect comparisons between observational studies. The ESC agreed with the evaluation that the presented evidence was not reliable, and remains inconclusive, given the high risk of bias and confounding associated with the comparisons. The evaluation considered that a cautious conclusion based on the totality of the evidence is that the effectiveness and safety profiles of Spikevax and Comirnaty appear to be similar. However, recognising the naïve nature of the indirect comparisons, interval analyses of effectiveness indicated that the effectiveness against COVID-19 -related hospitalisation for Comirnaty appeared to be more stable than that for Spikevax over time. The ESC considered that waning VE for Spikevax was a key uncertainty, and the

comparison of Spikevax with Comirnaty was more uncertain over longer time periods due to the limited clinical data for Spikevax to inform this comparison.

6.86 While noting the uncertainties described above (paragraph 6.85), the ESC considered that a claim that Spikevax is non-inferior to Comirnaty in terms of comparative effectiveness and safety in the requested NIP populations was reasonable. The ESC noted that the broader evidence review conducted by the ATAGI also supported this view (see paragraph 2.8).

6.87 The clinical evidence such as that based on the XBB.1.5-adapted vaccines may have limited applicability in the current Australia setting given that this variant does not represent the current predominant circulating SARS-CoV-2 variants in Australia. NB.1.8.1 (under monitoring) is the current dominant SARS-CoV-2 variant (14 July to 10 August 2025) accounting for 72.2% of sequences in Australia. Small numbers of sequences of other variants under monitoring, including XFG, LP.8.1 of SARS-CoV-2[19].

6.88 The PBAC considered that the claim of superior effectiveness compared with no vaccination was reasonable, although the magnitude of benefit and the duration of benefit were uncertain given the observational nature of the available evidence and limited evidence to estimate VE in the requested populations over longer time periods. However, the PBAC also noted that the conclusion of superior effectiveness was only appropriate if the delay which has impacted the TGA evaluation of Spikevax LP.8.1 is satisfactorily resolved (see paragraph 2.1).

6.89 The PBAC considered that the claim of inferior safety compared with no vaccination was reasonable. The PBAC noted that the safety of Spikevax was supported by randomised clinical trials and real-world experience with earlier Spikevax vaccines, as described in the ATAGI advice and TGA-approved product information documents.

6.90 The PBAC noted the limitations of the evidence informing the indirect comparison of Spikevax and Comirnaty, and the concerns raised by the evaluation and the ESC as described above. Overall, the PBAC advised that it would be reasonable to consider the Spikevax mRNA-1273 vaccine platform across strains and seasons as non-inferior to the Comirnaty BNT162b2 vaccine platform with respect to effectiveness and safety, when corresponding versions of the vaccines are compared, e.g. Spikevax LP.8.1 compared with Comirnaty LP.8.1. The PBAC noted this conclusion was consistent with ATAGI advice. The PBAC considered that the future VE of Spikevax would be dependent upon availability of updated variant vaccines on an ongoing basis for the NIP. As such, a conclusion of non-inferior effectiveness is only appropriate if the delay which has impacted the TGA evaluation of Spikevax LP.8.1 is satisfactorily resolved (see paragraph 2.1). The PBAC noted that Comirnaty LP.8.1 was granted TGA approval on 1 October 2025 (see paragraph 2.4).

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19 https://www.health.gov.au/sites/default/files/2025-08/australian-respiratory-surveillance-report-28-july-to-10-august-2025.pdf

Economic analysis

6.91 The submission presented a modelled economic evaluation of Spikevax compared with no vaccine for the prevention of COVID-19. Relative reduction in COVID-19 infections and hospitalisations is derived from a large observational study of mRNA-1273 (Spikevax) targeting the KP.2 SARS-CoV2 variant (Wilson et al 2025[20]). Consistent with the claim of superior effectiveness and inferior safety to no vaccine, the economic evaluation was a cost-effectiveness / cost-utility analysis.

6.92 The evaluation reported that the submission's description of the economic approach was inadequate. Many steps and assumptions in the model were not well explained, were poorly justified or not discussed in the submission. The submission did not discuss the applicability of inputs for the model, did not identify alternative sources for inputs, nor justified why some sources have been used instead of more recent or more applicable sources. In many cases, the model functions could only be identified by evaluators by tracing the inputs of the model through to sources, as the submission did not provide adequate documentation. Despite the availability of Australian estimates of hospitalisation and deaths, the submission provided only superficial attempts at validating the model accuracy (and did not include deaths in this approach, which would have uncovered a considerable flaw in the model). An extensive re-specified base case that corrects key errors, and applies more reasonable parameter estimates, was proposed during the evaluation. The ESC's advice is summarised in paragraphs 6.122 to 6.129.

Table 20: Summary of model structure, key inputs and rationale

Component	Summary	Evaluation comments
Treatments	Spikevax vs no updated vaccine.	The model compares Spikevax with no recent vaccination. Comirnaty is a near market comparator, and a cost-minimisation approach of Spikevax and Comirnaty may be a reasonable approach if non-inferiority is established.
Time horizon	1 year for estimating the consequences of vaccination. Life years and QALYs lost due to early death due to COVID-19 are estimated over the remaining life expectancy of patients.	This is reasonable. However, to fully estimate the impact of vaccination, the model only includes vaccine uptake in the first 6 months of the model for most patients. Although this is artificial, including uptake across the full year would have resulted in considerable loss of benefit as VE would continue into the subsequent year and not be captured.
Outcomes	Life-years gained and quality adjusted life years gained. The model also presents clinical outcomes such as hospitalisation and outpatient cases.	This is reasonable.

[20] Wilson, A, Bogdanov, A, Zheng, Z, Ryan, T, Zeng, N, Joshi, K, Lu, T, Bonafede, M & Araujo, AB 2025, 'Evaluating the Effectiveness of 2024-2025 Seasonal mRNA-1273 Vaccination Against COVID-19-Associated Hospitalizations and Medically Attended COVID-19 among adults aged≥ 18 years in the United States', *medRxiv*, p. 2025.2003. 2027.25324770.

Component	Summary	Evaluation comments
Methods used to generate results	Decision tree with cohorts separated by age.	The approach could have been simpler. Vaccine uptake and COVID-19 cases are simulated monthly over 1 year which is a complex approach. The results were presented for the overall population only, and not for each requested population.
Counterfactual model incidence	COVID-19 hospitalisations, infections and impact of recent vaccination	AIHW 2023-24 hospitalisation data for COVID-19, converted to infections using Le et al 2025[21], effect of recent vaccination removed using vaccine coverage from NNDSS data, VE from Wilson et al 2025[22] and rVE from Kavidondala et al 2024[23].
Health states	No infection, infection, dead. The infection health state has several possible consequences that are associated with different utilities and costs. These include no care, outpatient care, inpatient care, ICU, ventilator, readmission, long-COVID and mortality. See model structure (Figure 3-1, p120 of the submission).	Conceptually, the health states appear reasonable. However, non-hospitalised health states may not align with the purpose of COVID-19 vaccinations, which is to reduce the risk of severe disease and death. The non-hospitalised health states are significant drivers of the model results. The evidence required to inform the membership of the nominated health states is disparate, may not be sufficiently transitive, and may not be applicable to the estimate of VE applied in the model.
Transition probabilities	Various sources for the no vaccine arm. VE influences the rate of infections and hospitalisations, and this is sourced from a U.S. cohort study.	The model estimates the incidence of COVID-19, the likelihood of hospitalisation and downstream impacts. These estimates are primarily sourced from Australian publications (including Australian Department of Health publications). The vaccine only has an impact on the number of COVID-19 cases or hospitalisations. All other downstream transitions remain constant.
Health related quality of life	QALY decrements are estimated for COVID-19 cases, hospitalisations, consequences of hospitalisation and post-COVID-19.	Some sources of estimates for QALY decrements may not be applicable to current circulating variants of COVID-19.

Source: Table 3-1, p114 of the submission.
AIHW = Australian Institute for Health and Welfare; COVID = Coronavirus disease of 2019; ICU = Intensive Care Unit; NIP = National Immunisation Program; NNDSS = National Notifiable Diseases Surveillance System; QALY = Quality-Adjusted Life Year; rVE = relative vaccine effectiveness; VE = Vaccine effectiveness.

6.93 The submission applied a 1 year time horizon to estimate the impact of Spikevax on COVID-19 cases and hospitalisations. Infections were estimated per month, and

[21] Le, TP, Conway, E, Akpan, E, Abell, IR, Abraham, P, Baker, CM, Campbell, PT, Cromer, D, Lydeamore, MJ & McDonough, Y 2025, 'Health impact and cost-effectiveness of COVID-19 booster vaccination strategies in the early post-Omicron era: a dynamic modelling study', *BMJ Global Health*, vol. 10, no. 9.
[22] Wilson A, Rahai N, Beck E, Beebe E, Conroy B, Esposito D, et al. Evaluating the Effectiveness of mRNA-1273.815 Against COVID-19 Hospitalization Among Adults Aged≥ 18 Years in the United States. Infectious Diseases and Therapy. 2025;14(1):199-216.
[23] Kavikondala, S, Haeussler, K, Wang, X, Bausch-Jurken, MT, Nassim, M, Mishra, NK, Malmenäs, M, Sharma, P, Van de Velde, N, Green, N & Beck, E 2024, 'Comparative Effectiveness of mRNA-1273 and BNT162b2 COVID-19 Vaccines Among Older Adults: Systematic Literature Review and Meta-Analysis Using the GRADE Framework', *Infect Dis Ther*, vol. 13, no. 4, Apr, pp. 779-811.

vaccine uptake was estimated per month. The submission only included vaccine uptake for the first 6 months of the 12 month model duration for those populations that only receive 1 dose per year (18-64 and 65-74 year cohorts). For the 75+ year cohort, a second dose is assumed to fall in the latter half of the model duration. The approach is not realistic, but may be a reasonable simplification. By including all vaccinations at the beginning of the modelled year, the vaccine has sufficient time to prevent COVID-19 cases and hospitalisations prior to VE wanes. If vaccinations had been simulated over the full year, vaccinations administered toward the end of the model time horizon would incur the full cost of the vaccination, but achieve fewer avoided COVID-19 cases or hospitalisations as these consequences may occur in the following year. The model assumes that a minority of the 75+ year cohort will receive 2 doses (27% of 75+ year olds are estimated to receive the vaccine. Of those, 43.3% will receive a second dose corresponding to 11.7% of 75+ year olds) which does not reflect the requested NIP listing which requests biannual doses for this age group.

6.94 The populations included in the model are aged 18-64 with severe immunocompromise (assumed to be 3.76% of the total 18-64 year age cohort), aged 65-74, and aged ≥75 years. The model includes age specific COVID-19 infection rates, age specific COVID-19 hospitalisation rates and age specific VE estimates. The model did not include estimates of uptake or effectiveness in the Aboriginal and Torres Strait Islander population aged 50-64 years and was therefore inconsistent with the proposed NIP listing.

6.95 Cumulative vaccine uptake rates used in the model are presented below in Table 21. Altering the uptake of vaccine by month has the potential to change the ICER within the corresponding age group. Altering the uptake of vaccine in a way that changes the proportional use of Spikevax across different age groups has the potential to change the weighted ICER, since the cost-effectiveness of Spikevax varies by age group.

Table 21: Cumulative vaccine uptake for Spikevax by age group (%) in the economic model

Age group		Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb
18-64		3.5	12.5	25.1	38.4	44.1	46.9	46.9	46.9	46.9	46.9	46.9	46.9
65-74		2.7	8.8	15.0	21.2	24.3	25.9	27.1	27.1	27.1	27.1	27.1	27.1
75-100		2.7	8.8	15.0	21.2	24.3	25.9	27.1	27.1	27.1	27.1	27.1	27.1
75-100 2nd dose		0.0	0.0	0.0	0.0	0.0	0.0	1.3	2.8	4.2	6.5	9.1	11.7

Source: Table 3-14, p128 and Table 3-15, p129 of the submission.

6.96 The overall modelling approach was to create a counterfactual estimate of COVID-19 infections, hospitalisations and consequences (such as ICU attendance, use of ventilation, COVID-19 death and long-COVID) that would have occurred in the absence of the availability of a vaccine. This approach started with hospitalisation rates based on AIHW FY 2023-24 data, and back-calculated infections using published ratio of

infections to hospitalisations[24]. Cases were separated into hospitalisations (and into non-ICU, ICU and ventilation), outpatient attendances and no formal care, all stratified by the age brackets described above. The model was calibrated to AIHW hospitalisations at this point.

6.97 The submission used estimated vaccine coverage and VE (derived using Australian vaccination data, published estimates of VE and an assumed market share between Spikevax and Comirnaty) to calculate the number of infections and hospitalisations that would have occurred in the absence of vaccinations in the community. This final step was not included in the model and could not be verified during the evaluation. However, the evaluation noted that predictions from the counterfactual model (infections, hospitalisations and deaths) could be roughly compared with Australian estimates as a method of validation.

Table 22: Base case incidence of symptomatic infection in the no vaccine arm (no updated COVID-19 formulation vaccine within the last 6-12 months) in the model

Age Group	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb
18-64 years	2.89%	4.47%	6.13%	5.69%	3.22%	2.19%	2.13%	2.46%	4.61%	4.68%	5.34%	3.21%
65-74 years	1.92%	2.92%	3.89%	3.55%	2.00%	1.36%	1.32%	1.53%	2.88%	2.92%	3.35%	2.03%
75+ years	3.86%	5.87%	7.82%	7.13%	4.01%	2.73%	2.66%	3.08%	5.79%	5.88%	6.74%	4.09%

Source: Table 3-10, p126 of the submission.
COVID = Coronavirus disease of 2019.

6.98 The ESC agreed with the evaluation that the submission had used several estimates to inform the counterfactual model that were inappropriate or applied incorrectly in the model, including:

- The submission assumed 30% of deaths will occur at home (70% in hospital). This was based on a study of patients (primarily with cancer and chronic diseases) who had been in contact with palliative care who died during the early years of the COVID-19 pandemic[25]. The study was not applicable to the way it was used in the model. More importantly, the model removed 30% of patients from Australian estimates of COVID-19 mortality (ABS) to estimate in-hospital deaths, and they were not included in the model at all.
- Mortality was estimated from an ABS report on deaths due to COVID-19. Mortality was estimated from July 2021 to June 2022, and included 6,988

[24] Le, TP, Conway, E, Akpan, E, Abell, IR, Abraham, P, Baker, CM, Campbell, PT, Cromer, D, Lydeamore, MJ & McDonough, Y 2025, 'Health impact and cost-effectiveness of COVID-19 booster vaccination strategies in the early post-Omicron era: a dynamic modelling study', *BMJ Global Health*, vol. 10, no. 9.
[25] Lobb, E, Maccallum, F, Phillips, JL, Agar, M, Hosie, A, Breen, LJ, Tieman, J, DiGiacomo, M, Luckett, T & Philip, J 2024, 'The COVID-19 Pandemic: Bereavement Experiences Between Hospital and Home Deaths in Palliative Care', *Journal of Pain and Symptom Management*, vol. 67, no. 2, pp. 147-156.

deaths from COVID. The evaluation considered it was unclear why this period was used. Mortality from COVID-19 has been falling over time. Estimated mortality was 6,190 in 2023, 5,103 in 2024 and 3,252 in the 24-25 financial year.

- Deaths were distributed across age groups; however an error was made during this process resulting in too few deaths being attributed to the 65-74 year age group.
- The submission applied a 7.78% post-discharge mortality rate based on a meta-analysis reporting all-cause mortality over 1 year in patients hospitalised with COVID-19[26]. The submission applied this inconsistently in the model. Firstly, the model applied a post-discharge rate of 6.59% rather than 7.78%. The discrepancy was not explained and appeared to be an error. Secondly, the in-hospital mortality was reduced by 7.78% (to 92.22% of mortality). However, the model then applied 6.59% as a mortality rate to all hospitalisations to estimate post-discharge mortality. This increased the mortality rate in the model by approximately 16 fold, 7 fold and 60% in the 18-64, 65-74 and 75-100 year age groups. Stated in another way, for every person that dies in hospital in the 18-64 age group, 16 die after discharge. The evaluation noted this is inappropriate.
- The model applies 17.86% readmissions based on an Australian study of hospital re-presentations[27]. This was inappropriate as the AIHW hospitalisation data used to calibrate hospitalisations already incorporated re-admissions. The approach taken in the model represents double counting.

6.99 The submission did not provide adequate discussion relating to the validity of the model. The model base case overestimated COVID-19 infections and mortality from COVID-19. The evaluation stated that excluding readmissions from the base case may result in a more reasonable estimate of hospitalisations.

[26] Ramzi, ZS 2022, 'Hospital readmissions and post-discharge all-cause mortality in COVID-19 recovered patients; A systematic review and meta-analysis', *The American journal of emergency medicine*, vol. 51, pp. 267-279.

[27] Ling, T, Basic, D, Tcharkhedian, E, Campisi, J, Pringle, B & Khoo, A 2024, 'Care in the Community: A COVID-19 initiative to reduce hospital re-presentations among community-dwelling people', *Australasian Journal on Ageing*, vol. 43, no. 3, pp. 474-481.

Table 23: Comparison of the model comparator arm and Australian estimates

Outcome	Model base case (comparator arm)	Comparison estimate	Source of comparison
Symptomatic infections	2,430,722	1,371,448[b]	NNDSS dashboard reported COVID-19 infections for 2022
Hospitalisations (including readmissions)	74,055 (98,644)	74,711[a]	AIHW COVID-19 separations FY 2023-24
COVID-19 deaths	11,205	6,988	ABS COVID-19 deaths for FY2021-22

Source: generated during the evaluation from the Spikevax economic model
ABS = Australian Bureau of Statistics; AIHW = Australian Institute of Health and Welfare; COVID = Coronavirus disease of 2019; FY = Financial Year; NNDSS = National Notifiable Diseases Surveillance System.
[a]Estimated by multiplying hospitalisations in the 18-64 age group by 3.76%.
[b]Estimated by multiplying cases in the 18-64 age group by 3.76%.

6.100 Overall, the submission base case contains a number of errors or poorly justified parameters that overestimate symptomatic infections and mortality. The evaluation considered that the submission base case was reasonably well calibrated to hospitalisations (after removal of readmissions) but was not calibrated to plausible estimates of either symptomatic infections or mortality.

6.101 The ESC agreed with the evaluation that the model considerably overestimated symptomatic infections, hospitalisations and COVID-19 deaths. Reported COVID-19 infections were highest in Australia in 2022. There was mandatory reporting during this period and it was likely that a substantial proportion of infections that were captured were mild or asymptomatic. It was also likely that circulating virus variants were more likely to result in symptomatic disease in 2022, as hospitalisations appear to have reduced over time. The evaluation discussed that once reported 2022 estimates were adjusted to reflect the model population, it was clear that the model overestimated infections because the model estimated symptomatic infections much higher than indicated by Australian data for 2022. The evaluation considered that the model's estimate of hospitalisation was an overestimate due to double-counting of readmissions, but appears reasonable if readmissions were excluded. The model considerably overestimated mortality from COVID-19 (the model estimated COVID-19 deaths much higher than indicated by Australian data for FY2021-22). This was partly due to the error associated with post-discharge mortality. However in addition, ABS estimates of COVID-19 mortality have fallen since FY2021-22.

6.102 The evaluation considered that the hospitalisation rates for the populations aged ≥65 years were appropriately derived. However, the hospitalisation rates for the 18-64 year age group reflected hospitalisations for the whole Australian population (aged 18-64 years) rather than just the immunocompromised population. The evaluation noted that if individuals with immunocompromise are more likely to be hospitalised with COVID-19, the model may underestimate hospitalisations for this population.

- The submission applied an estimate of VE for infections and for hospitalisations in the model. VE was sourced from an observational study (Wilson et al 2025[28]) which used a matched cohort approach to estimate VE of the KP.2 vaccine administered in August-December 2024 against COVID-19. VE was estimated at 64 days post-vaccination and was 52.8% (95% CI 34.8%, 65.8%) against COVID-19 related hospitalisations and 39.4% (95% CI 35.0%, 43.5%) against medically attended COVID-19. Estimates of VE were slightly higher for older age groups, and age specific estimates were used in the model. The estimates of VE for hospitalisations and for infections were sourced from a single study. The evaluation noted that estimates of VE vary across studies for different vaccine strains and different circulating variants. Model estimates were therefore uncertain as future VE is likely to vary. Estimates of VE applied in the model are presented in Table 24. The ESC recalled that the Comirnaty submission had estimated VE from a broader evidence base (Raxtozinameran May 2025 PSD, Table 10). The ESC advised that despite differences in model design, there was no rationale for the modelled benefits estimated in the Spikevax model to exceed the estimates accepted by the PBAC for the Comirnaty model in December 2025 for the matching populations, given there was no evidence to support a difference in clinical effectiveness between the vaccines.

Table 24: Vaccine effectiveness included in the model

Vaccine effectiveness outcome	Published estimate (median day 57+7 days)	Waning rate per month	Estimated VE at 14 days post vaccination
Infections			
18+ years, high risk	40.4%	4.75%	48.2%
65+ years	46.7%%		54.5%
Hospitalisation			
18+ years, high risk	46.5%	2.46%	50.54%
65+ years	53.2%		57.24%

Source: generated from "VE.Interventions.COVID" tab of the Spikevax economic model. VE derived from Wilson et al 2025[29]. Waning derived from Andersson et al 2024[30] and Higdon et al 2022[31].
VE = Vaccine effectiveness.

[28] Wilson, A, Bogdanov, A, Zheng, Z, Ryan, T, Zeng, N, Joshi, K, Lu, T, Bonafede, M & Araujo, AB 2025, 'Evaluating the Effectiveness of 2024-2025 Seasonal mRNA-1273 Vaccination Against COVID-19-Associated Hospitalizations and Medically Attended COVID-19 among adults aged≥ 18 years in the United States', *medRxiv*, p. 2025.2003. 2027.25324770.
[29] Wilson, A, Bogdanov, A, Zheng, Z, Ryan, T, Zeng, N, Joshi, K, Lu, T, Bonafede, M & Araujo, AB 2025, 'Evaluating the Effectiveness of 2024-2025 Seasonal mRNA-1273 Vaccination Against COVID-19-Associated Hospitalizations and Medically Attended COVID-19 among adults aged≥ 18 years in the United States', *medRxiv*, p. 2025.2003. 2027.25324770.
[30] Andersson, NW, Thiesson, EM, Pihlstrom, N, Perala, J, Faksova, K, Gram, MA, Poukka, E, Leino, T, Ljung, R & Hviid, A 2024, 'Comparative effectiveness of monovalent XBB.1.5 containing covid-19 mRNA vaccines in Denmark, Finland, and Sweden: target trial emulation based on registry data', *BMJ Med*, vol. 3, no. 1, p. e001074.
[31] Higdon, MM, Baidya, A, Walter, KK, Patel, MK, Issa, H, Espie, E, Feikin, DR & Knoll, MD 2022, 'Duration of effectiveness of vaccination against COVID-19 caused by the omicron variant', *Lancet Infect Dis*, vol. 22, no. 8, Aug, pp. 1114-1116.

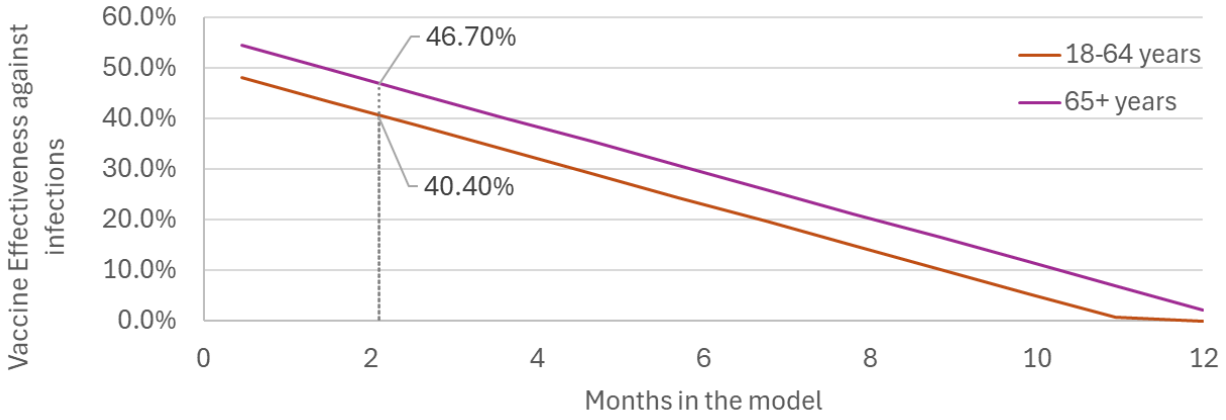
6.103 The submission translated the estimate of VE from Wilson et al 2025 to reflect what VE would have been at 14 days post vaccination. This was done by applying an estimate of waning for VE for hospitalisations (2.46% per month) and for VE for infections (4.75% per month) from two separate studies (Andersson et al 2024[32] and Higdon et al 2022[33]). This approach assumed that VE wanes linearly from a peak at 14 days post-vaccination. This was not justified in the submission. Estimates of VE over time in the model are presented in Figure 5 and Figure 6.

6.104 Estimates of waning were sourced from studies separate to the study used for estimating VE (Wilson et al 2025). Applying the estimates of waning to the initial model VE results in minimal VE against infections remaining at 12 months, but considerable VE against hospitalisations remaining at 12 months. Median follow up in Wilson et al 2025 was 57 days (follow up was estimated from 7 days post vaccination). Waning against hospitalisations was derived from a target trial emulation based on registry data and reported estimates out to 24 weeks from vaccination with a monovalent XBB.1.5 containing COVID-19 mRNA vaccine not limited to Spikevax (Andersson et al 2024). Waning against infections was derived from a systematic review and meta-analysis that reported estimates out to 6 months and was not limited to Spikevax (Higdon et al 2022). The evaluation considered that the model's estimates of longer-term VE for Spikevax were highly uncertain. The ESC considered that the model's estimates were implausible, noting that Figure 6 indicated ongoing VE against hospitalisations at 12 months which was not supported by clinical evidence.

[32] Andersson, NW, Thiesson, EM, Pihlstrom, N, Perala, J, Faksova, K, Gram, MA, Poukka, E, Leino, T, Ljung, R & Hviid, A 2024, 'Comparative effectiveness of monovalent XBB.1.5 containing covid-19 mRNA vaccines in Denmark, Finland, and Sweden: target trial emulation based on registry data', *BMJ Med*, vol. 3, no. 1, p. e001074.

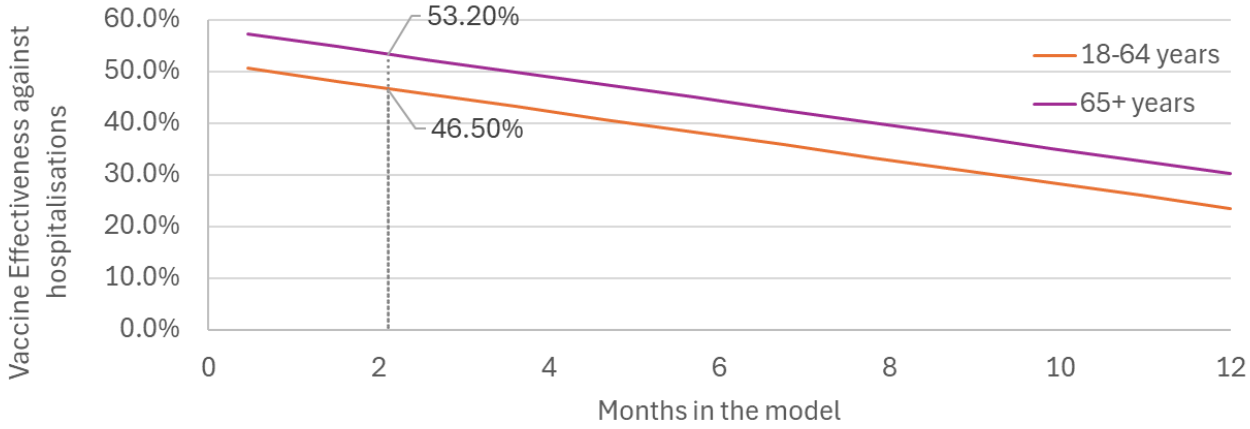
[33] Higdon, MM, Baidya, A, Walter, KK, Patel, MK, Issa, H, Espie, E, Feikin, DR & Knoll, MD 2022, 'Duration of effectiveness of vaccination against COVID-19 caused by the omicron variant', *Lancet Infect Dis*, vol. 22, no. 8, Aug, pp. 1114-1116.

Figure 5: Vaccine effectiveness against infections, assuming maximum vaccine effectiveness at 14 days post-vaccination



Source: Derived from table 3-16, p129 of the submission.
Data points represent the VE measured in Wilson et al 2025 (the source of the VE) and represents Day 64. Vaccine effectiveness is linearly extrapolated backwards to day 14.

Figure 6: Vaccine effectiveness against hospitalisations, assuming maximum vaccine effectiveness at 14 days post-vaccination



Source: Derived from table 3-16, p129 of the submission.
Data points represent the VE measured in Wilson et al 2025 (the source of the VE) and represents Day 64. Vaccine effectiveness is linearly extrapolated backwards to day 14.

6.105 The evaluation noted that VE estimates (and waning estimates), impacted the number of avoided infections and avoided hospitalisations. Costs and QALY decrements were applied to infections, hospitalisations and consequences of infections and hospitalisations and were therefore directly proportional to the VE applied in the model.

6.106 The submission applied QALY decrements for infections, hospitalisations, admission to ICU, requirement for ventilation, COVID-19 related myocarditis, vaccine adverse events, death due to COVID-19, and post-acute infection. The model results were

highly sensitive to QALY decrements applied due to early COVID-19 death, and QALY decrements applied to all infections and hospitalisations following acute COVID-19. The evaluation reported that the magnitude of the QALY decrements applied in both of these cases was inappropriate.

6.107 The model estimated QALY decrements for COVID-19 deaths based on age-specific Australian population life-expectancy and age-specific population norms for utility values (not adjusted for underlying health status). However, the evaluation noted that patients who die from COVID-19 commonly have underlying health conditions. Wouterse et al 2025[34] estimated that life years lost and QALYs lost following a COVID-19 death were approximately 37% lower and 47% lower when adjusting for underlying health conditions compared with population average estimates. The PSCR disagreed with the use of Wouterse et al 2022 to adjust LYs and QALYs lost, suggesting the results were not applicable to the proposed NIP populations. The ESC considered that Wouterse et al 2022 could be used to approximate QALYs lost as proposed by the evaluation (Table 25), although noted this would not be a precise estimate.

Table 25: Adjusting lost LYs and QALYs in the Spikevax economic model to account for underlying health status

Age group	Life-years (LYs) Lost	Adjusted for underlying health status[a]	Quality-adjusted life-years (QALYs) Lost	Adjusted for underlying health status[b]
18-64 years	17.50	11.08	14.98	7.91
65-74 years	11.59	7.34	10.06	5.31
75-100 years	5.30	3.35	4.55	2.40

Source: generated from Wouterse et al 2022 and "QALYs" tab of the Spikevax economic model.
LY = life-years; QALY = quality-adjusted life-years
[a]Wouterse et al 2022 reported life years lost for men and women based on average life-expectancy, and recalculated life years lost after adjusting for underlying health status. Adjusted life-years losses were 63% of what was calculated using average life-expectancy.
[b]Wouterse et al 2022 reported quality adjusted life years lost for men and women based on average life-expectancy and average age specific utility values. Adjusted QALY losses were 53% of what was calculated using average life-expectancy and average age specific utility values.

6.108 The model applied a QALY decrement to every patient with either an infection or hospitalisation to reflect a loss of quality of life following the acute phase of COVID-19. The QALY decrement applied to patients experiencing a COVID-19 infection was derived from a study that followed nonhospitalised patients for 6 months up to December 2020[35]. The QALY decrement applied to patients experiencing a COVID-19 hospitalisation was derived from a study that followed patients hospitalised between

[34] Wouterse, B, Ram, F & van Baal, P 2022, 'Quality-adjusted life-years lost due to COVID-19 mortality: methods and application for the Netherlands', *Value in Health*, vol. 25, no. 5, pp. 731-735.
[35] Sandmann, FG, Tessier, E, Lacy, J, Kall, M, Van Leeuwen, E, Charlett, A, Eggo, RM, Dabrera, G, Edmunds, WJ & Ramsay, M 2022, 'Long-term health-related quality of life in non-hospitalized coronavirus disease 2019 (COVID-19) cases with confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in England: longitudinal analysis and cross-sectional comparison with controls', *Clinical Infectious Diseases*, vol. 75, no. 1, pp. e962-e973.

March 2020 and April 2021 for up to a year[36]. The evaluation considered that estimates from these studies were prone to bias. Participants were identified following infection and asked to recall their health status prior to infection. Not all patients were followed up in the study, and the authors acknowledged that those patients that continued to have symptoms may have been more likely to have answered the follow up questionnaire. Furthermore, the circulating virus during the period of the study was likely to have been more severe (did not include omicron) and treatments for COVID-19 were less available. Post-acute QALY decrements account for about 40% of the model incremental QALYs. The ESC has previously noted that it is reasonable to exclude the impact of vaccination on long-COVID (Table 14, raxtozinameran, PSD, May 2025 PBAC Meeting). The ESC noted that the Spikevax model included long COVID impacts over the year subsequent to an infection and considered that the estimate was not reliable. The ESC considered this should be removed as per the evaluator's respecified base case given the limited data to estimate the impact.

6.109 The ESC noted that following the acute loss of quality of life due to symptomatic infection or hospitalisation, the submission applied an additional QALY decrement to all patients based on EQ-5D estimates over 6 months or 12 months following infection or hospitalisation. The evaluation noted these estimates were prone to bias, and likely not applicable to the present day. The ESC considered the estimates were unreliable due to low completion rate, and significant recall bias, and noted that the ICER was sensitive to the assumed effect. Accordingly, the ESC advised that the QALY decrements for post-infection cases should be removed from the model base case. The ESC considered that higher quality data would be needed to support inclusion in the economic model, and noted this was unlikely to be available.

Table 26: QALY decrements associated with post-COVID-19 infection applied in the model

Model parameter	QALY decrement	Source
COVID infection, not hospitalised	0.028	Sandmann et al 2022
COVID hospitalisation.	0.122	Evans et al 2022

Source: Table 3-21, p131 of the submission.
COVID = Coronavirus disease of 2019; QALY = Quality-Adjusted Life Year.

6.110 The submission included costs associated with vaccination procurement, vaccination administration, adverse events, infection related myocarditis, outpatient care (including emergency department visits), in-patient care, and ongoing care associated

[36] Evans, RA, Leavy, OC, Richardson, M, Elneima, O, McAuley, HJ, Shikotra, A, Singapuri, A, Sereno, M, Saunders, RM & Harris, VC 2022, 'Clinical characteristics with inflammation profiling of long COVID and association with 1-year recovery following hospitalisation in the UK: a prospective observational study', *The Lancet Respiratory Medicine*, vol. 10, no. 8, pp. 761-775.

with long-COVID. The decision to include infection related myocarditis was not well justified, however this was not a driver of the model results.

6.111 The evaluation considered that as the submission included only Grade 3 adverse events, the average cost per Grade 3 adverse event of $14.87 appears to be low. Grade 3 events are "Severe" adverse events that typically prevent daily activity and require medical intervention based on the standard toxicity grading scale used for vaccine trials (Chu 2021[37]). The evaluation respecified base case assumed that a Grade 3 event requires at least one GP visit, costed at MBS item 23. The PSCR did not accept this change, arguing that the evaluation had overestimated the proportion of individuals that would visit a GP. The PSCR argued that according to the AusVax Safety database, less than 1% of vaccinated individuals reported visiting a GP after receiving a COVID-19 vaccine. However, the ESC noted that the cited AusVax safety report refers to 0.9% of all vaccinated individuals reporting a visit to GP or emergency department, which does not reflect the rate for individuals who experienced Grade 3 (Severe) adverse events[38].

6.112 The evaluation suggested that the submission had underestimated the cost of hospitalisations in the model. Hospitalisations were derived using 2025-26 NEP price weights for nominated AR-DRGs (E62A and E62B for hospitalisations, E40A, E40B, E41A and E41B for ICU and ventilation). However, COVID-19 hospitalisations may have a longer average length of stay compared with that of the AR-DRGs used to estimate hospitalisation costs. AIHW reported an average length of stay for all COVID separations of 12 days, 31 days for separations involving ventilation and 24 days for separations involving ICU 2023–24[39]. However, AR-DRGs used to determine the cost of COVID hospitalisations, ICU and ventilations have average lengths of stay ranging from 3 days to 12 days. In several cases, the AIHW estimated length of stay exceeded the inlier bounds for ALOS for the nominated AR-DRGs. The evaluation found that increasing hospitalisation costs to reflect longer average hospital stays had a moderate impact on the model. However, the ESC noted that the PBAC had previously considered costs of COVID-19 hospitalisation when considering the cost-effectiveness evaluation for Comirnaty in May 2025 and December 2025. The ESC advised that the Spikevax model should use consistent values, since the PBAC had given recent advice on these specific inputs. The ESC noted that median length of stay for separations with

[37] Chu L, McPhee R, et al.; mRNA-1273 Study Group. A preliminary report of a randomized controlled phase 2 trial of the safety and immunogenicity of mRNA-1273 SARS-CoV-2 vaccine. Vaccine. 2021 May 12;39(20):2791-2799. doi: 10.1016/j.vaccine.2021.02.007. Epub 2021 Feb 9.

[38] COVID-19 vaccine safety data – at a glance, as at 12 May 2025. Based on surveys sent on day 3 post vaccination (includes any vaccine currently being used, not specific to Spikevax). https://www.ausvaxsafety.org.au/vaccine-safety-data/covid-19-vaccines

[39] https://www.aihw.gov.au/hospitals/topics/admitted-patient-care/hospitalisations-involving-a-covid-19-diagnosis

a COVID-19 diagnosis in 2023–24 was 4 days[40], and considered the AR-DRGs costs applied by the submission were reasonable and were consistent with the costs previously accepted for COVID-19 hospitalisations (Raxtozinameran May 2025 PSD, Table 10).

6.113 The evaluation noted there were a number of key drivers in the model. It noted that the estimates of VE for infections and hospitalisations (estimated for the KP.2 variant of Spikevax) were key drivers, and had been derived from an observational study. and the duration of VE applied in the model (a product of estimates of waning effectiveness) was uncertain and may not be reasonable.

6.114 Many issues included in the table below are not uncertain, but represent errors in the model, inappropriate use of data, or use of less applicable data when more recent data were available. These issues were addressed in an evaluation re-specified base case.

Table 27: Issues noted by the evaluation

Description	Method/Value	Impact Base case: $[redacted]/QALY gained
Readmissions	The submission includes 17.86% of all hospitalisations resulting in readmissions. Readmissions in the model only add costs and do not affect mortality or QALYs. The hospitalisation rate in the model is calibrated to AIHW hospitalisation data. The inclusion of 17.86% readmissions represents double-counting.	Moderate, favours Spikevax. Removing readmissions from the base case increases the ICER by [redacted]%. This parameter is more influential after errors are corrected in the model. **Inappropriate use of data.**
VE	The submission estimates VE at 7 days post-vaccination based on an assumed linear rate of waning. If initial waning is slower or non-linear, the initial VE may not be as high.	Moderate, favours Spikevax. Assuming that the published estimate of VE (average follow up of 64 days) is correct for the first 2 months of the model results in a [redacted]% increase in the ICER. **Uncertain.**
Overall mortality	The submission base case has used ABS COVID-19 mortality estimates from FY2021-22, which reported 6,988 deaths. More recent estimates indicate a reduction in mortality from COVID-19. The FY2024-25 ABS data reported 3,252 deaths from COVID-19.	High, favours Spikevax. Using more recent estimates of mortality to derive mortality rates results in an increase in the ICER of approximately [redacted]%[a]. **Use of older data when newer estimates are available.**
Post-discharge mortality	The submission has assumed that 6.59% of all patients hospitalised, regardless of age group, will die following discharge[b]. This estimate is based on 1 year all-cause mortality reported in a meta-analysis. The model has already been calibrated to Australian COVID-19 deaths. Although the model 'accounts' for a post-discharge percentage in the in-hospital deaths, it does so inappropriately.	High, favours Spikevax. Removing post-discharge mortality from the base case increases the ICER by [redacted]%[c]. **Inappropriate use of data / error.**

[40] Excel file, Admitted patient care 2023–24 Separations with a COVID-19 diagnosis.xls available at https://www.aihw.gov.au/hospitals/topics/admitted-patient-care/hospitalisations-involving-a-covid-19-diagnosis

Description	Method/Value	Impact Base case: $[1]/QALY gained
COVID-19 death LYs and QALYs	The submission assumes that death from COVID-19 incurs a loss of life years and QALYs based on average life expectancy and average age-specific utilities. Patients who die of COVID-19 tend to have underlying health conditions. Adjusting for this results in a smaller loss of LYs and QALYs.	High, favours Spikevax. Adjusting for the health status of patients who die from COVID-19 increases the ICER by [redacted]% **Incomplete data.**
Post-COVID QALY decrements	Following the acute loss of quality of life due to symptomatic infection or hospitalisation, the submission has applied an additional QALY decrement to all patients based on EQ-5D estimates over 6 months or 12 months following infection or hospitalisation. These estimates are prone to bias, and not likely applicable to the present day.	High, favours Spikevax. Removing post-COVID QALY decrements from the model increases the ICER by [redacted]%. **Highly uncertain.**
Out-of-hospital mortality	The model has derived mortality rates from ABS data. During the derivation, 70% of mortality was assumed to occur in hospital (or post-discharge) and 30% was assumed to occur at home. There is no evidence that the 30% removed from the in-hospital mortality rate has been included in the model. This is likely an error.	High, disfavours Spikevax. Adding the 30% mortality back into the estimates of mortality in the model reduces the ICER by [redacted]%[d]. **Error.**

Source: constructed during the evaluation.
ABS = Australian Bureau of Statistics; AIHW = Australian Institute of Health and Welfare; AR = Adverse reaction; COVID = Coronavirus disease of 2019; ICER = Incremental cost-effectiveness ratio; ICU = Intensive Care Unit; QALY = Quality-Adjusted Life Year; VE = Vaccine effectiveness.
aThis analysis includes a minor correction of an error in which deaths were incorrectly allocated to the wrong age bracket when estimating rates. The correction moves more deaths onto the 65-74 age group from the 75+ age group, and the correction of this error alone would decrease the ICER.
bThe model input sheet derives 7.78%, however 6.59% is applied in the model. This is likely an error.
cThis analysis also corrects the mortality rates derived for in-hospital deaths so that 100% of deaths are now in-hospital (rather than 92.22%, as applied in the base case). The post-discharge mortality rate is applied in the base case such that it is not 7.78% (or 6.59%) of all mortality, but 7.78% of all hospitalisations.
dThis omission has a greater impact on the model after the post-discharge mortality error has been corrected.
The redacted values correspond to the following ranges:
[1] *$25,000 to < $35,000*

6.115 The submission base case resulted in an incremental cost effectiveness ratio of $25,000 to < $35,000 per additional QALY (or per fewer QALYs lost due to COVID-19). The submission did not present a stepped analysis. Disaggregated outcomes and costs are presented below. The ESC considered that the submission's base case was not reliable for decision making.

Table 28: Clinical outcomes, disaggregated outcomes and disaggregated costs from the submission base case comparing Spikevax with no vaccination

Outcome	No recent COVID-19 vaccine	Spikevax	Difference
Number Vaccinated	0	1,888,455	1,888,455
Number of Vaccine Doses Administered	0	1,888,455	1,888,455
Clinical outcomes			
Symptomatic Infections	2,430,722	2,236,711	-194,011
Hospitalisations	83,698	75,122	-8,576
Readmissions	14,941	13,410	-1,531
COVID-related Deaths	11,205	10,054	-1,151
Infection Related Myocarditis	1,547	1,424	-124
Adverse Event Myocarditis	0	10	10
Long COVID	85,841	78,970	-6,871
QALY losses			
Infection-Related Mortality	60,412	54,208	-6,203
Infection-Related Morbidity	66,802	61,304	-5,497
AE-Related Morbidity	0	186	186
Total QALYs Lost	127,213	115,698	-11,515
Costs			
Vaccination (including AEs)†	$0	$[redacted]	$[redacted]
Hospitalisation (including recovery)	$1,048,711,110	$941,261,952	-$107,449,158
Short-term non-hospitalised patient care	$259,054,999	$238,831,763	-$20,223,236
Post-acute care	$66,105,414	$59,419,470	-$6,685,944
COVID 19-infection-related myocarditis cases	$13,719,898	$12,623,432	-$1,096,466
Total costs	$1,387,591,421	$[redacted]	$[redacted]
Incremental cost effectiveness ratio			
Cost / LY gain			**$[redacted][1]**
Cost / QALY gain			**$[redacted][2]**

Source: Table 3-36, p138, Table 3-33, p137, Table 3-34, p138, Table 3-35, p138 of the submission.
AE = Adverse Event; COVID = Coronavirus disease of 2019; QALY = Quality-Adjusted Life Year.
The redacted values correspond to the following ranges:
[1] *$45,000 to < $55,000*
[2] *$25,000 to < $35,000*

6.116 As previously noted, the base case model predicted a very high number of symptomatic infections in the target population of 18-64 year old patients with severe immunocompromise, and patients aged ≥65 years. The evaluation noted that the model estimates were considerably higher than the highest Australian estimates from NNDSS.

6.117 The evaluation noted that sensitivity analyses presented by the submission should be interpreted with caution because many parameters would have a larger impact on the model than it appeared, if other parameters that are key drivers were corrected for the analysis (data not shown).

6.118 The commentary has performed univariate sensitivity analyses addressing key issues identified during the evaluation. Justifications for the sensitivity analyses and advice

from the ESC are presented in the table below. In addition to the changes shown in Table 29, the PSCR made additional changes (see paragraphs 6.122 and 6.123).

Table 29: Description of the sensitivity analyses applied during the evaluation, with justifications

#	Parameter and base case	Sensitivity analysis	Reason for change / justification	PSCR	ESC advice
Transitions / proportions					
#1	Readmissions = 17.86% of all hospitalisations	0%	**Error** Initial hospitalisations in the model have been calibrated to AIHW hospitalisations, which already capture re-admissions. The use of readmissions in the model appear to be double counting.	Change accepted by PSCR.	Input for sensitivity analysis supported by ESC
#2	Initial VE derived by assuming linear waning	Assume no waning in the first two months	**Unsupported** The submission has increased the initial VE based on an assumption that waning estimates can be linearly extrapolated back from 64 days to 14 days.	Not addressed.	Input for sensitivity analysis supported by ESC, however there is no justification for assuming higher VE for Spikevax compared with Comirnaty
#3	Long Covid = 9.6% post hospitalisation, 4.7% post outpatient	0%	**Unsupported** The impact of vaccination on long-COVID is not presented in the submission.	Change not accepted by PSCR but additional discussion provided and revised inputs applied (see paragraph 6.23).	Input for sensitivity analysis supported by ESC
#4	ICU 5.74%, ventilation 5.78% of hospitalisations	AIHW based ICU and CVS per age group (assume that all CVS occur in ICU)	**More reasonable source of estimate** AIHW reports separations requiring mechanical ventilation and ICU from 2023-24. These estimates are lower than Hitch et al 2024 used in the submission. Hitch et al reported on hospitalisations up to November 2021 and likely represents more severe disease.	Change accepted by PSCR.	Input for sensitivity analysis supported by ESC

#	Parameter and base case	Sensitivity analysis	Reason for change / justification	PSCR	ESC advice
#5	COVID-19 mortality based on 2021-22 data.	Corrected error in model, and update mortality to ABS values from 2024-25	**More reasonable source of estimate** The submission incorrectly distributed mortality across age brackets. The correction does not alter the estimate of deaths but moves deaths from the 75-79 age group to the 65-74 age group. ABS data from 2024-25.	Change partially accepted by PSCR.	Input for sensitivity analysis supported by ESC
#6	Post-discharge mortality = 6.59%	Removed from the model as incorrectly applied. Hospital related deaths are inflated by 1/92.22%.	**Error** The correction reflects an earlier calculation in the submission, and is required to ensure that the model is consistent with ABS deaths.	Change partially accepted by PSCR.	Input for sensitivity analysis supported by ESC
Health outcomes					
#7	LY and QALYs gained based on population life expectancy and utility norms	Estimate LYs and QALYs based on reduced health in those prone to severe COVID	**Unreasonable assumption** This correction uses Wouterse et al 2022 that reported LYs lost and QALYs lost adjusted for health status. Approximately 63% LYs and 53% QALYs of population norms	Change not accepted by PSCR.	Pending PBAC advice
#8	QALY decrements related to post-COVID-19 condition 0.28 for infections, 0.122 for hospitalisation	Remove post-COVID-19 QALY decrements	**Potentially biased estimate** QALY decrements are already included for infections and hospitalisations. The studies upon which long term QALY decrements are sources are prone to bias and represent COVID-19 during earlier, less applicable virus strains.	Change not accepted by PSCR but additional discussion provided and revised inputs applied (see paragraph 6.23)	Input for sensitivity analysis supported by ESC
Costs					
#9	Emergency department costs = $841.39	922.86	**Error** Model error / discrepancy with submission. Corrected cost is weighted average of E2080A and E2080B.	Change accepted by PSCR.	Input for sensitivity analysis supported by ESC
#10	Non-ICU costs: $9,001. ICU costs: $23,150. Ventilation costs: $23,150.	Non-ICU costs: $16,289. ICU costs: $22,434. Ventilation costs: $33,520.	**More reasonable estimate** Increase admission costs and mechanical ventilation costs to reflect that average LOS for COVID-19 is considerably longer than AR-DRGs.	Change accepted by PSCR.	Input for base case supported by ESC

#	Parameter and base case	Sensitivity analysis	Reason for change / justification	PSCR	ESC advice
#11	Adverse event costs = $14.87 per Grade 3 event	Adverse event costs = $43.90	Assume that a Grade 3 event requires at least one GP visit, costed at MBS item 23.	Change not accepted by PSCR.	Input for sensitivity analysis supported by ESC
Scenario					
#12	Inclusion of costs and outcomes associated with non-hospitalised infections (both outpatient and no formal care)	Remove all influence of COVID-19 cases that are not hospitalised.	**Uncertain** The greatest uncertainty in the model relates to the estimate of infections. The overall estimate of infections appears implausible. ATAGI advice recommended that the value of a vaccine for COVID-19 should be driven by severe COVID-19, as indicated by hospitalisations and mortality. The PSD for Comirnaty indicates that the sponsor for Comirnaty did not include infections - only hospitalisations. It is not possible to "turn infections" off in the model, and challenging to remove all infection related costs and outcomes - however the VE for infections can be set to zero which will retain the VE for hospitalisation but remove incremental differences in costs / outcomes for non-hospitalised cases.	Change not accepted by PSCR but additional discussion provided and revised inputs applied (see paragraph).	Input for sensitivity analysis supported by ESC
#13	70% of deaths occur in hospital (or post-discharge), 30% occur outside of hospital	Include 100% mortality	**Possibly an error** When estimating mortality rates, the submission assumes 30% would occur out of hospital and reduces mortality rates in hospital to 70% of the ABS mortality rates. However, the evaluation cannot identify where out of hospital deaths are reintroduced into the model and they appear to have been overlooked. The sensitivity analysis inflates in-hospital deaths to account for 100% mortality.	Change accepted by PSCR.	Input for sensitivity analysis supported by ESC

Source: generated during the evaluation.
ABS = Australian Bureau of Statistics; AIHW = Australian Institute of Health and Welfare; AR = Adverse reaction; ATAGI = Australian Technical Advisory Group on Immunisation; COVID = Coronavirus disease of 2019; CVS = Continuous ventilatory support; GP = General practitioner; ICU = Intensive Care Unit; LOS = Length of Stay; MBS = Medicare Benefits Schedule; PSD = Public summary document; QALY = Quality-Adjusted Life Year; VE = Vaccine effectiveness.

6.119 The results of the evaluation univariate sensitivity analyses are presented below.

Table 30: Univariate sensitivity analyses performed during the evaluation

#	Sensitivity analysis	Incremental costs	Incremental QALYs	ICER	Change
	Base case	$[redacted]	11,515	$[redacted][1]	
Transitions / proportions					
#1	Readmissions = 0%	$[redacted]	11,477	$[redacted][1]	[redacted]%
#2	Published VE used at start (no back calculation to estimate highest VE)	$[redacted]	10,727	$[redacted][1]	[redacted]%
#3	Remove long-COVID costs from the model	$[redacted]	11,515	$[redacted][1]	[redacted]%
#4	Reduce % of hospitalisations requiring ICU and ventilation to AIHW estimates	$[redacted]	11,494	$[redacted][1]	[redacted]%
#5	Change mortality to reflect ABS estimates for 2024-25	$[redacted]	10,251	$[redacted][1]	[redacted]%
#6	Correct post-discharge mortality in the model	$[redacted]	8,591	$[redacted][2]	[redacted]%
Health outcomes					
#7	LY and QALY losses adjusted for health status	$[redacted]	8,587	$[redacted][2]	[redacted]%
#8	Remove QALY decrements applied to infections or hospitalisations after acute phase	$[redacted]	6,940	$[redacted][3]	[redacted]%
Costs					
#9	Correct Emergency Department costs	$[redacted]	11,515	$[redacted][1]	-[redacted]%
#10	Increase hospitalisation costs by applying AR-DRGs with higher average LOS	$[redacted]	11,515	$[redacted][4]	-[redacted]%
#11	Increase cost of Grade 3 AE to one GP visit	$[redacted]	11,515	$[redacted][1]	[redacted]%
Scenario analysis					
#12	Remove effect of non-hospitalised cases in the model (both benefits and costs)	$[redacted]	6,893	$[redacted][3]	[redacted]%
#13	Add 30% mortality to account for out of hospital deaths	$[redacted]	12,666	$[redacted][1]	-[redacted]%

Source: generated during the evaluation based on the Spikevax economic model.
ABS = Australian Bureau of Statistics; AE = Adverse Event; AIHW = Australian Institute of Health and Welfare; AR = Adverse reaction; COVID = Coronavirus disease of 2019; GP = General practitioner; ICER = Incremental cost-effectiveness ratio; ICU = Intensive Care Unit; LOS = Length of Stay; QALY = Quality-Adjusted Life Year; VE = Vaccine effectiveness.
The redacted values correspond to the following ranges:
[1] *$25,000 to < $35,000*
[2] *$35,000 to < $45,000*
[3] *$45,000 to < $55,000*
[4] *$15,000 to < $25,000*

6.120 The commentary proposed a respecified base case as shown in Table 31. Further scenarios that were recommended by the ESC are also shown.

Table 31: Proposed respecified base case and further scenarios

	Incremental costs	Incremental QALYs	ICER	Difference from base case and change from prior step
Submission Base case	**$[redacted]**	**11,515**	**$[redacted][1]**	**0**
#1: Readmissions = 0%	$[redacted]	11,477	$[redacted][1]	[redacted]%: inc [redacted]%
+ #6: Correct post-discharge mortality in the model	$[redacted]	8,553	$[redacted][2]	[redacted]%: inc [redacted]%
+ #13: Add 30% mortality to account for out of hospital deaths	$[redacted]	9,892	$[redacted][2]	[redacted]%: dec [redacted].%
+ #9: Correct Emergency Department costs	$[redacted]	9,892	$[redacted][2]	[redacted]%: dec [redacted]%
+ #4: Reduce % of hospitalisations requiring ICU and ventilation to AIHW estimates	$[redacted]	9,874	$[redacted][2]	[redacted]%: inc [redacted]%
+ #5: Change mortality to reflect ABS estimates for 2024-25	$[redacted]	7,777	$[redacted][3]	[redacted]%: inc [redacted]%
+ #7: LY and QALY losses adjusted for health status	$[redacted]	6,629	$[redacted][4]	[redacted]%: inc [redacted]%
+ #10: Increase hospitalisation costs by applying AR-DRGs with higher average LOS	$[redacted]	6,629	$[redacted][3]	[redacted]%: dec [redacted]%
+ #11: Increase cost of Grade 3 AE to one GP visit	$[redacted]	6,629	$[redacted][3]	[redacted]%: inc [redacted]%
+ #8: Remove QALY decrements applied to infections or hospitalisations after acute phase	$[redacted]	1,967	$[redacted][6]	[redacted]%: inc [redacted]%
RESPECIFIED BASE CASE (RBC)	**$[redacted]**	**1,967**	**$[redacted][6]**	
Respecified base case AND removal of the effect of non-hospitalised cases	$[redacted]	1,259	$[redacted][7]	[redacted]% increase over RBC
ESC Scenarios				
ESC scenario 1 Applies all 13 changes identified in evaluation	$[redacted]	1,200	$[redacted][7]	[redacted]% increase over RBC
ESC scenario 2 Applies all changes identified in evaluation except #7	$[redacted]	2,301	$[redacted][5]	[redacted]% decrease from RBC
ESC scenario 3 Do not apply the changed hospitalisation costs (#10), but apply all other changes identified in evaluation	$[redacted]	1,200	$[redacted][7]	[redacted]% increase over RBC
ESC scenario 4 Do not apply #7, and do not apply the changed hospitalisation costs (#10), but apply all other changes identified in evaluation	$[redacted]	2,301	$[redacted][6]	[redacted]% increase over RBC

Source: generated during the evaluation.

ABS = Australian Bureau of Statistics; AE = Adverse Event; AIHW = Australian Institute of Health and Welfare; AR = Adverse reaction; GP = General practitioner; ICER = Incremental cost-effectiveness ratio; ICU = Intensive Care Unit; LOS = Length of Stay; QALY = Quality-Adjusted Life Year; RBC = respecified base case.

The redacted values correspond to the following ranges:

[1] *$25,000 to < $35,000*
[2] *$35,000 to < $45,000*
[3] *$45,000 to < $55,000*
[4] *$55,000 to < $75,000*
[5] *$135,000 to < $155,000*
[6] *$155,000 to < $255,000*
[7] *$255,000 to < $355,000*

6.121 The respecified base case resulted in an ICER of $155,000 to < $255,000 per additional QALY. There are several changes to the base case that reduce the ICER (such as reintroducing 30% mortality and increasing hospitalisation costs), and several changes that increase the ICER (such as correcting readmissions, correcting the application of post-discharge mortality, using more recent mortality rates and adjusting for health status when calculating LY and QALY losses due to COVID-19 deaths). The step with the largest impact on the model results is the removal of long-term QALY decrements applied to all infections and hospitalisations.

- Outstanding areas of uncertainty include the emphasis that the model places on infections rather than hospitalisations. In the re-specified base case, nearly 40% of all QALY losses are associated with outpatient cases or no formal treatment cases. Excluding QALYs lost to mortality, more than 80% of QALY losses are associated with non-hospitalised COVID-19 infections. Excluding non-hospitalised infections from the model entirely would increase the re-specified base case ICER from $155,000 to < $255,000 to $255,000 to < $355,000, primarily driven by a reduction in the incremental QALYs. The PSCR acknowledged that reducing severe disease is the primary public health objective, however did not agree with the removal of non-hospitalised cases in the model. The ESC agreed with the evaluation that non-hospitalised infections were overestimated by the submission model, e.g. there were 485,833 reported cases of COVID-19 in people aged 75+ in 2022 and the model estimated 1,356,427 cases. This is about 3 fold higher than the highest reported number of cases for this age group. The ESC noted that a very large proportion of the incremental QALYs accrued in the model were derived from patients infected but not hospitalised (#12). Removing the effect of non-hospitalised cases will remove GP and ED costs, and also remove the QALY decrements that are applied in step #8 (see Table 30). The ESC agreed with the ATAGI that modelling symptomatic COVID-19 cases was not appropriate for the purposes of the economic evaluation given the high degree of uncertainty it introduced, and that the relevant clinical outcomes for the model were hospitalisations, ICU admissions and deaths (see paragraph **Error! Reference source not found.**). The ESC noted that the incremental QALYs in the model are substantially driven by non-hospitalised COVID-19 infections. The ESC advised that modelling symptomatic COVID-19 cases was not appropriate given the high degree of uncertainty it introduced, noting that definitions varied between studies. The ESC advised it may be appropriate to remove all influence of COVID-19 cases that are not hospitalised, as proposed in the evaluation, which would be more conservative than the sponsor's base case.

6.122 The PSCR presented a revised base case with an aggregate ICER of $35,000 to < $45,000/QALY. The revised base case accepted only 7 of the 13 changes proposed in the evaluation's respecified base case (including 2 changes that were only partially accepted) as noted in Table 29. The PSCR reported ICERs for the individual populations of $15,000 to < $25,000/QALY in the 75+ population, $55,000 to < $75,000 /QALY in the 65-74 year population, and $95,000 to < $115,000 /QALY in the 18-64 severe IC and 50-64 ATSI population.

6.123 The evaluation provided a respecified base case with an ICER of $155,000 to < $255,000/QALY, and an analysis excluding the impact of non-hospitalised infections entirely from the respecified base case results in an ICER of $255,000 to < $355,000/QALY, which the ESC believed to be more reliable than the submission base case of $25,000 to < $35,000/QALY. The ESC noted that the PSCR had provided a respecified base case with an ICER of $35,000 to < $45,000/QALY. The ESC considered that while this updated figure accepted some of the 13 changes proposed during the evaluation, it still contained key limitations which meant the ICER remained under-estimated and uncertain, and it introduced new uncertainties due to extensive changes made in the PSCR model. Given these uncertainties and in light of the extensive changes in the PSCR that had not been evaluated, the ESC advised that the PSCR model was not reliable for decision making.

6.124 The ESC advised that the evaluation's respecified base case together with removal of the effect of non-hospitalised cases ($255,000 to < $355,000/QALY) would be informative for PBAC decision-making, although noted that there were remaining concerns to be considered by the PBAC and suggested the additional model scenarios presented in Table 31.

6.125 Despite the range of amendments proposed by the evaluation, the ESC considered that major uncertainties remained including: 1) ongoing uncertainty relating to future VE and vaccine waning in each population; and 2) vaccine utilisation assumptions across populations which impact the overall ICER.

6.126 The ESC considered that the submission's approach to modelling was reasonable in principle (although unnecessarily complex), however noted that serious concerns had been raised in the evaluation regarding the inputs applied in the model. The ESC advised that the revisions presented by the evaluators increased the reliability of the model, however there were uncertainties that could not be tested and revised given the model structure, including the parameters used for VE and waning. The ESC advised the issues/options raised in paragraphs 6.119 to 6.123 relating to the model inputs/parameters should be explored further and would likely require re-evaluation.

6.127 The ESC noted the model did not include estimates of uptake or effectiveness in the Aboriginal and Torres Strait Islander population aged 50-64 years and was therefore inconsistent with the proposed NIP listing.

6.128 Comirnaty is a near market comparator. The ESC considered there was no rationale to support more favourable assumptions for Spikevax in the economic evaluation compared with the assumptions accepted for the Comirnaty economic evaluation in December 2025. The ESC considered the current submission had overestimated VE and did not sufficiently consider uncertainty of future VE given the platform approach. The ESC recalled the PBAC advised in its May 2025 consideration of Comirnaty, that for a platform approval, the economic evaluation would need to provide confidence that the platform will be cost-effective and likely to remain cost-effective in most future years, including if considered across a cycle of many years. As such, the ESC advised that more conservative estimates of VE would be required.

6.129 The ESC agreed with the evaluation, that a cost-minimisation approach of Spikevax and Comirnaty may be a reasonable approach if non-inferiority is established.

6.130 The pre-PBAC response provided a discussion about model issues including VE and waning; vaccination coverage; Long COVID; Post-Discharge Mortality and Symptomatic infection. The response defended the inputs in the sponsor's economic model and did not effectively address the concerns raised by the ESC about the need for more conservative inputs in a model for a platform approval.

6.131 The pre-PBAC response stated that a nationally cost-effective price is expected to be determined from the resolution of the inputs and options raised from Moderna's economic model or through a cost-minimisation to Comirnaty on a dose equivalence basis.

Vaccine cost/patient

6.132 The price of Spikevax proposed in the submission was $[redacted] per dose. Under the proposed NIP listing, patients <75 years of age would be eligible for one annual dose, and patients ≥75 years of age would be eligible for two annual doses (the economic model assumed 43.3% of those that receive a first annual dose will receive a second dose, however the utilisation model assumed 100% would receive a second dose: this discrepancy was not justified).

Estimated NIP usage & financial implications

6.133 This submission was not considered by DUSC.

6.134 The submission used an epidemiological approach to estimate the number of incident patients who would be eligible for Spikevax. A summary of the data sources and parameter values used to estimate the utilisation and financial impacts associated with the proposed listing of Spikevax for the prevention of COVID-19 is shown in Table 32. The submission did not consider the near market comparator, Comirnaty in the utilisation and financial estimates.

Table 32: Key inputs for financial estimates

Incident 1: Population aged 65-74: People (2025-2030)						
Eligible patients	2,632,258	2,703,641	2,775,585	2,843,186	2,904,151	2,949,269
Uptake - all treatment	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%
Treated patients	[redacted][9]	[redacted][10]	[redacted][10]	[redacted][10]	[redacted][10]	[redacted][10]
Incident 2: Population aged 75 years + (summer booster): People (2025-2030)						
Eligible patients	2,277,688	2,375,494	2,470,901	2,568,077	2,662,861	2,759,426
Uptake - all treatment	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%
Treated patients	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]
Incident 3: Population aged 18-64 years severely immunocompromised: People (2025-2030)						
Eligible patients	621,321	629,312	636,965	644,406	651,612	658,953
Uptake - all treatment	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%
Treated patients	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]
Incident 4: Population aged 75 years + (winter booster): People (2025-2030)						
Eligible patients	2,277,688	2,375,494	2,470,901	2,568,077	2,662,861	2,759,426
Uptake - all treatment	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%
Treated patients	[redacted][6]	[redacted][7]	[redacted][7]	[redacted][7]	[redacted][7]	[redacted][7]
Incident 5: First nations individuals aged 50-64: People (2025-2030)						
Eligible patients	130,885	131,926	132,684	133,295	134,141	134,891
Uptake - all treatment	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%
Treated patients	[redacted][1]	[redacted][1]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Doses - proposed vaccine						
	Year 1	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Year 6**
Spikevax – Incident 1	[redacted][9]	[redacted][10]	[redacted][10]	[redacted][10]	[redacted][10]	[redacted][10]
Spikevax – Incident 2	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][5]	[redacted][5]	[redacted][5]
Spikevax – Incident 3	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]
Spikevax – Incident 4	[redacted][6]	[redacted][7]	[redacted][7]	[redacted][7]	[redacted][7]	[redacted][8]
Spikevax – Incident 5	[redacted][1]	[redacted][1]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Total scripts	[redacted][11]	[redacted][11]	[redacted][11]	[redacted][11]	[redacted][11]	[redacted][11]
Net financial impact of Spikevax						
NIP	$[redacted][13]	$[redacted][13]	$[redacted][13]	$[redacted][14]	$[redacted][14]	$[redacted][14]
Net financial impact						
NIP impact	$[redacted][13]	$[redacted][13]	$[redacted][13]	$[redacted][14]	$[redacted][14]	$[redacted][14]
MBS impact	$[redacted][12]	$[redacted][12]	$[redacted][12]	$[redacted][12]	$[redacted][12]	$[redacted][12]
NIP/MBS impact	**$[redacted][14]**	**$[redacted][14]**	**$[redacted][14]**	**$[redacted][14]**	**$[redacted][14]**	**$[redacted][14]**

Source: The financial estimates from the submission: 2a. Patients - incident; 2d. Patients - DTG; 3a. Scripts - proposed; 3b. Impact - proposed (pub); 4a. Scripts - affected; 4b. Impact - affected (pub); 5. Impact - net; 7. Net changes - MBS.
MBS = Medicare Benefits Schedule; NIP = National Immunisation Program.
The redacted values correspond to the following ranges:
[1] *40,000 to < 50,000*
[2] *50,000 to < 60,000*
[4] *200,000 to < 300,000*
[5] *300,000 to < 400,000*
[6] *500,000 to < 600,000*
[7] *600,000 to < 700,000*
[8] *700,000 to < 800,000*
[9] *900,000 to < 1,000,000*

[10] *1,000,000 to < 2,000,000*
[11] *2,000,000 to < 3,000,000*
[12] *$50 million to < $60 million*
[13] *$400 million to < $500 million*
[14] *$500 million to < $600 million*

6.135 The total NIP impact of listing Spikevax was estimated to be $500 million to < $600 million in Year 6, and a total of > $1 billion in the first 6 years of listing based on the requested price. The ESC noted this was based on the populations and dosing regimens requested in the submission, which are more restrictive than current arrangements under the NCVP.

6.136 The submission used an epidemiological approach to estimate the utilisation of vaccination in each of the NIP populations. The populations included were:

- People aged 65-74
- People aged 75 years +
- People aged 18-64 years severely immunocompromised
- First Nations people aged 50-64

6.137 All patients were drawn from the current ABS Population Projections, Australia 2022-2071, except the Aboriginal and Torres Strait Islander population that was drawn from the ABS Projected population, Aboriginal and Torres Strait Islander peoples, States and Territories, 2021 to 2031 PSNS using the medium fertility, paternity and expectancy assumptions. This was appropriate however as noted in the evaluation, the populations were drawn from different sources, and there may be an overlap between the severe immunocompromised patients and the First Nations patients.

6.138 The population sources were appropriate; however, the financial model estimates commenced in 2025 which was inappropriate as the submission will not be presented to the PBAC until 2026. The populations in the model should be updated to cover 2026 to 2031.

6.139 The submission indicated that the uptake rates applied in each population were derived from the COVID-19 vaccination data published by the Department (October 2025). These data provide details of the number of vaccinations by age cohort in a rolling 12 months. The financial model assumed that the rate of vaccination would not be impacted by the listing of Spikevax. The evaluation considered that uptake rates are affected by two opposing changes; firstly, vaccination rates are continuing to decline, and distinct “seasons” are becoming less obvious in the data. Secondly, as noted by the evaluation, it is uncertain if the introduction of a new vaccine will increase the uptake of COVID-19 vaccines. While the uptake rate was drawn from an appropriate source, it was likely to be overestimated. The dosing regimen for 75+ years patients assumes that all patients will receive both annual vaccinations. This is unlikely to occur in clinical practice and so overestimates the number of vaccinations provided

6.140 The submission’s uptake rates are significantly higher than the current coverage information reported in the National Centre for Immunisation Research and

Surveillance (NCIRS) Annual Vaccination Coverage Report 2024 for comparable age cohorts.

6.141 The submission applied a rate of 3.76% from MacIntyre et al (2018) to the number of people 18-64 years who were immunocompromised. The evaluation considered it was uncertain if this rate can be generalised to the whole Australian population (geographically) due to the method and assumptions used to construct it. It is also unlikely that a single rate would apply across all age cohorts.

Quality Use of Medicines

6.142 The submission indicated that the sponsor's support of healthcare professionals that was commenced during the pandemic will continue with the listing of Spikevax on the NIP.

6.143 The post marketing surveillance currently provided by AusVaxSafety for all NIP-listed vaccines will continue. The submission did not identify any additional post marketing surveillance that the sponsor would undertake.

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

7 PBAC Outcome

7.1 The PBAC deferred making a recommendation for the National Immunisation Program (NIP) listing of the mRNA-1273 platform (Spikevax®) vaccines, for prevention of coronavirus disease 2019 (COVID-19) caused by SARS CoV-2 virus in four populations of adults as requested by the sponsor. The PBAC deferred making a recommendation due to the TGA evaluation of Spikevax LP.8.1. being delayed and the TGA Delegate's Overview not being available. The submission requested NIP listing for: 1) Adults aged 75 years or more (2 doses per year); 2) Adults aged 65-74 years (1 dose per year); 3) Adults aged 18-64 years with severe immunocompromise (1 dose per year); and 4) Aboriginal and Torres Strait Islander adults aged 50 to 74 years (1 dose per year). This represents a restricted group in comparison to current arrangements under the National COVID-19 Vaccination Program (NCVP). The PBAC considered that Spikevax was superior to no vaccine in terms of effectiveness with an acceptable safety profile, although the magnitude and duration of benefit were uncertain. The PBAC noted the limitations of the evidence, but overall concluded that it would be reasonable to consider the Spikevax mRNA-1273 vaccine platform non-inferior to the Comirnaty BNT162b2 vaccine platform with respect to effectiveness and safety, when corresponding versions of the vaccines are compared, e.g. Spikevax LP.8.1 compared with Comirnaty LP.8.1. The PBAC considered that the submission did not provide a reliable estimate of the cost-effectiveness of Spikevax versus no vaccination. However, the PBAC advised that if the near market comparator, Comirnaty, is listed on the NIP, and the TGA approve Spikevax LP.8.1 , Spikevax would be cost-effective if it were cost-minimised to Comirnaty for the requested populations.

7.2 The submission requested NIP listing of mRNA-1273 (Spikevax) vaccines updated to target circulating and emerging variants of SARS-CoV-2. As such, the proposed listing is not limited to the current TGA-approved version of Spikevax (JN.1), nor the version of Spikevax under consideration by the TGA currently (LP.8.1). A platform approach would mean that PBAC advice could apply to future adaptations of the mRNA-1273 (Spikevax) vaccine, manufactured by Moderna using the same platform, that have been approved by the TGA.

7.3 The PBAC noted that the reason for taking a platform approach to the consideration is to enable the efficient and timely introduction of future Spikevax vaccines to ensure the community has access to the latest vaccine through the NIP. As such, TGA registration of the latest vaccine is required. While earlier version of Spikevax, such as Spikevax XBB.1.5 and Spikevax JN.1 have been approved by the TGA, at the time of the March 2026 PBAC meeting, the most current version of Spikevax was the LP.8.1 variant adapted COVID 19 vaccine, which was still under evaluation by the TGA.

7.4 The PBAC considered it was important to use vaccines that target current variants of the COVID-19 virus (SARS-CoV-2). At the time of the March 2026 PBAC meeting, the most current version of Spikevax was the LP.8.1 variant adapted COVID-19 vaccine, for which the TGA evaluation was ongoing. The PBAC noted that new adapted vaccines are anticipated in the future. The PBAC noted that to support a platform approval, it would be necessary to consider suitable inputs for assessing cost effectiveness in the context of the additional uncertainty associated with the platform approach. Consistent with its previous advice for Comirnaty, the PBAC advised that a conservative approach to modelling would be appropriate, given there will be a time lag between evolution of SARS-CoV-2 variants, subsequent development of a corresponding adapted Spikevax vaccine, and uncertainty of the effectiveness of such vaccines in the future. The estimates of VE over 12 months should also consider waning protection from vaccination and lower effectiveness from changes in circulating variants.

7.5 The PBAC noted and welcomed the advice from the ATAGI.

7.6 The PBAC noted and welcomed the input received from the Lung Foundation Australia and the Pharmaceutical Society of Australia that supported the proposed NIP listing of Spikevax.

7.7 The submission did not request NIP listing for individuals under 18 years or individuals over 18 years where the advice from the ATAGI was to “consider” a dose based on individual risk-benefit assessment. The PBAC acknowledged that a restricted program limited to a smaller group of high-risk individuals would reduce health outcomes at the population level in comparison with current arrangements under the NCVP. However, the PBAC considered it was reasonable to accept the proposed NIP listing, as this was consistent with advice from the ATAGI that emphasised that populations with medical risk conditions are heterogenous, and that ATAGI did not support an overall recommendation for vaccination in groups where its advice was to “consider” a dose based on individual risk-benefit assessment. The PBAC advised that broader

access would require further clarity in relation to the definition of the populations, and a cost-effectiveness evaluation.

7.8 The PBAC noted that no COVID-19 vaccines are currently included on the NIP, however recalled that it had recommended Comirnaty for NIP listing for the same four adult populations in December 2025. The PBAC considered that the submission's nomination of no vaccination as main comparator and Comirnaty as a near market comparator was appropriate, however should Comirnaty be listed on the NIP, Comirnaty adapted for the most recent variants would be the appropriate main comparator.

7.9 Overall, the PBAC advised that clinical effectiveness and safety had been demonstrated for Spikevax vaccines, noting that the TGA will remain responsible for evaluation and regulatory approval of future variant adapted vaccines before these are made available through the NIP. However, the PBAC also noted that the conclusion of superior effectiveness compared with no vaccine was only appropriate if Spikevax LP.8.1 is TGA approved. The PBAC noted that Comirnaty LP.8.1 was granted TGA approval in October 2025.

7.10 While the PBAC accepted that Spikevax is more effective than no vaccine, the PBAC considered that estimates of VE remain uncertain as there were several limitations associated with the observational and retrospective nature of the evidence presented. Further, the PBAC noted there were limited effectiveness data for individuals ≥75 years of age, and individuals who were severely immunocompromised. No data were presented for the proposed Aboriginal and Torres Strait Islander population. A key uncertainty was the lack of evidence regarding the duration of protection for Spikevax, which has implications for establishing duration of response, in particular for the 12-month period between doses.

7.11 The robustness of the comparison of Spikevax and Comirnaty was limited by the non-randomised observational nature of the evidence assessing VE. The PBAC noted the limitations of the evidence, but overall concluded that it would be reasonable to consider the Spikevax mRNA-1273 vaccine platform non-inferior to the Comirnaty BNT162b2 vaccine platform with respect to effectiveness and safety, when corresponding versions of the vaccines are compared, e.g. Spikevax LP.8.1 compared with Comirnaty LP.8.1.

7.12 In regard to the cost-effectiveness analysis for Spikevax versus no vaccination, the PBAC advised that the economic model presented in the submission was not suitable for decision making because although the revisions presented in the evaluation increased the reliability of the model, there were uncertainties that could not be tested or revised given the model structure, including the parameters used for VE and waning (see paragraph 6.126). The PBAC advised that a standard re-entry resubmission and re-evaluation would be required before the Spikevax economic model could be used for decision-making.

7.13 The PBAC noted the evaluation respecified base case resulted in an ICER of $155,000

to < $255,000/QALY, and a further analysis excluding the impact of non-hospitalised infections increased the ICER $255,000 to < $355,000/QALY. The PBAC considered the analysis excluding the non-hospitalised infections was more informative noting ESC's advice that modelling symptomatic COVID-19 cases was not appropriate given the high degree of uncertainty it introduced. Although the ICER for Spikevax versus no vaccination could not be reliably estimated, the PBAC noted that the model demonstrated it was unacceptably high and a substantial price reduction would be required for Spikevax to be considered cost-effective.

7.14 The PBAC advised that a cost-minimisation to Comirnaty would be reasonable if non-inferiority is accepted, pending TGA approval for Spikevax LP.8.1.

7.15 The PBAC considered that the method to generate the financial estimates in the submission was reasonable, although the results were uncertain as vaccine uptake is likely to vary, based on rates of COVID-19 infection and its perceived risk in the community. The submission estimated a total of approximately 2,000,000 to < 3,000,000 doses in Year 1 increasing to 2,000,000 to < 3,000,000 in Year 6 (**Table 32**), assuming Spikevax was the only COVID-19 vaccine listed on the NIP.

7.16 The PBAC noted that additional information would be required from the sponsor to support further consideration of Spikevax including confirmation of TGA approval of Spikevax LP.8.1. This would include an update on the TGA status of Spikevax LP.8.1. and any other vaccine updates submitted, or planned to be submitted to the TGA. The sponsor is asked to confirm its commitment to communicate with the Department, the TGA, and ATAGI in a timely manner, with the intent to provide the most up-to-date COVID 19 vaccine to Australians through the NIP.

7.17 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:
Deferred

8 Context for Decision

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

9 Sponsor's Comment

The sponsor had no comment.