Record of the Immunisation Advisory Committee Meeting held on 26 March 2024

Immunisation Advisory Committee records are published in accordance with the Terms of Reference for the Specialist Advisory Committees 2021.

Note that this document is not necessarily a complete record of the Immunisation Advisory Committee meeting; only the relevant portions of the meeting record relating to Immunisation Advisory Committee discussions about an application or Pharmac staff proposal that contain a recommendation are generally published.

The Immunisation Advisory Committee may:

(a) recommend that a pharmaceutical be listed by Pharmac on the Pharmaceutical Schedule and the priority it gives to such a listing;

(b) defer a final recommendation, and give reasons for the deferral (such as the supply of further information) and what is required before further review; or

(c) recommend that Pharmac decline to list a pharmaceutical on the Pharmaceutical Schedule.

Pharmac Advisory Committees make recommendations, including priority, within their therapeutic groups of interest.

The record of this Advisory Committee meeting will be reviewed by PTAC at an upcoming meeting.

Specialist Advisory Committees and PTAC may differ in the advice they provide to Pharmac, including recommendations' priority, due to the committees' different, if complementary, roles, expertise, experience, and perspectives.

Pharmac is not bound to follow the recommendations made below. Applications are prioritised by Pharmac against other funding options and progressed accordingly. The relative priority of any one funding choice is dependent on a number of factors, including (but not limited to) the recommendation of PTAC and/or Specialist Advisory Committees, the mix of other applications being assessed, the amount of funding available, the success of commercial negotiations and/or the availability of clinical data.

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1. Attendance

Present
Stephen Munn (Chair)
David Murdoch
Elizabeth Wilson
Erasmus Smit
Gary (Edwin) Reynolds
James Ussher (attended via Zoom)
Lance Jennings
Nikki Turner
Osman Mansoor
Stuart Dalziel

Apologies
Karen Hoare
Michael Tatley
Sean Hanna
Tony Walls

2. Summary of recommendations

Pharmaceutical and Indication	Recommendation
• Recombinant varicella zoster virus vaccine for the prevention of shingles	Provisional amendments to access criteria
• Comirnaty Adult XBB.1.5 vaccine (COVID-19 vaccine)	Amendment to the number of funded doses to align with Medsafe approved data sheet
• RSVPreF3 vaccine for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus for people aged 60 years and over	Deferred
• Moderna: Elasomeran, elasomeran and davesomeran, andusomeran vaccine (Spikevax) for the prevention of COVID-19	No formal recommendation
• Novavax: SARS-CoV-2 rS XBB1.5 vaccine (Nuvaxovid XBB1.5) for the prevention of COVID-19	No formal recommendation
• Pfizer: Tozinameran, riltozinameran, famtozinameran, raxtozinameran (BNT162b2) vaccine (Comirnaty®) for the prevention of COVID-19	No formal recommendation
• CSL-Seqirus: ARCT-154 for the prevention of COVID-19	No formal recommendation

3. The role of Specialist Advisory Committees and records of meetings

3.1. This meeting record of the Immunisation Advisory Committee is published in accordance with the Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) 2021 and Specialist Advisory Committees 2021.Terms of Reference describe, *inter alia*, the establishment, activities, considerations, advice, and the publication of such advice of Specialist Advisory Committees and PTAC.

3.2. Conflicts of Interest are described and managed in accordance with section 6.4 of the SAC Terms of Reference.

3.3. The Immunisation Advisory Committee is a Specialist Advisory Committee of Pharmac. The Immunisation Advisory Committee and PTAC and other Specialist Advisory Committees have complementary roles, expertise, experience, and perspectives. The Immunisation Advisory Committee and other Specialist Advisory Committees may therefore, at times, make recommendations for treatments for Immunisation that differ from PTAC's, including the priority assigned to recommendations, when considering the same evidence. Likewise, PTAC may, at times, make recommendations for treatments for Immunisation that differ from the Immunisation Advisory Committee's, or Specialist Advisory Committees may make recommendations that differ from other Specialist Advisory Committees'.

Pharmac considers the recommendations provided by both the Immunisation Advisory Committee and PTAC and any other relevant Specialist Advisory Committees when assessing applications for treatments for Immunisation.

4. Welcome and Introduction

4.1. The Chair welcomed the Committee with a karakia, followed by whakawhanaungatanga.

5. Record of Immunisation Advisory Committee meeting held Thursday, November 9, 2023

5.1. The Advisory Committee reviewed the minutes of the Immunisation Advisory Committee meeting held on Thursday, 9 November 2023 and agreed that the minutes be accepted.

6. Previous action points/recommendations made

6.1. The Committee noted epidemiological updates regarding invasive pneumococcal disease (IPD) and invasive meningococcal disease (IMD). The Committee noted that there is a significant delay in publication of IPD reports, but the incidence of serotype 19A cases remains of great concern and the epidemiology is changing every quarter. The Committee considered that young children with IPD have a very high health need and sequelae result in high health sector costs.

6.2. The Committee requested that the Public Health Agency work with Pharmac to provide timely epidemiology updates for each future meeting.

6.3. The Committee strongly reiterated the urgency of a catch-up programme for children up to 59 months of age who have not previously received any doses of PCV13 vaccine.

7. Pharmac Update

7.1. The Committee noted the Pharmac update.

8. Matters Arising: Recombinant zoster vaccine eligibility criteria for immunocompromised

Recommendations

8.1. The Committee recommended the access criteria for recombinant varicella zoster virus vaccine for the prevention of shingles be amended provisionally to the following (changes from the criteria the Committee recommended in November 2023, including provisional detail pending, in **bold**, deletions in ~~strikethrough~~):

> Recombinant varicella zoster vaccine [Shingles vaccine]
> Either:
> 1. Two doses for all people aged 65 years; or
> 2. Two doses for people 18 years of age and over with any of the following:
>   - **a. planning, receiving, or post CAR-T cell therapy; or**
>   - b. pre- or post-haematopoietic stem cell transplant; or
>   - c. solid organ transplant; or
>   - d. haematological malignancies; or
>   - e. people living with ~~poorly controlled~~ HIV infection; or
>   - f. planned or receiving ~~disease-modifying anti-rheumatic drugs (DMARDs)~~ **immune-modulating agents (pending specific agents/daily dose/duration/± any age aspects)** ~~for systemic lupus erythematosus, polymyalgia rheumatica or rheumatoid arthritis~~; or
>   - **g. planned or receiving high-dose corticosteroids (pending daily dose (in prednisolone-equivalents), duration ± age); or**
>   - h. end stage kidney disease (CKD 4 or 5); or
>   - i. primary immunodeficiency.

Discussion

8.2. The Committee noted that Pharmac staff had sought clinical advice from the Immunisation Advisory Committee at its November 2023 meeting about an application for the funding of recombinant varicella zoster (RVZV) vaccine for immunocompromised people 18 years of age and over.

8.3. The Committee noted that Pharmac staff had subsequently sought public consultation 15 February 2024 on a proposal to widen access to recombinant varicella zoster virus vaccine (branded as Shingrix) for prevention of shingles in immunocompromised people from 1 July 2024, using the access criteria previously recommended by the Committee in November:

> Recombinant varicella zoster vaccine [Shingles vaccine]
> Either:
> 1. Two doses for all people aged 65 years; or
> 2. Two doses for people 18 years of age and over with any of the following:
>   - a. pre- or post-haematopoietic stem cell transplant; or
>   - b. solid organ transplant; or
>   - c. haematological malignancies; or
>   - d. people living with poorly controlled HIV infection; or
>   - e. planned or receiving disease modifying anti-rheumatic drugs (DMARDs) for systemic lupus erythematosus, polymyalgia rheumatica or rheumatoid arthritis; or
>   - f. end stage kidney disease (CKD 4 or 5); or
>   - g. primary immunodeficiency

8.4. The Committee considered that the immunocompromised groups included in the proposed eligibility criteria had the same or greater risk of shingles incidence and severity as the currently eligible 65-year age group, based on available clinical evidence.

8.5. The Committee noted that consultation feedback requested the inclusion of people who are planning or receiving immune-modulating agents for a range of dermatology, rheumatology, gastroenterology indications.

8.6. The Committee noted Pharmac staff had sought advice via email from members of the Dermatology Advisory Committee regarding the groups with dermatological conditions, who are planning or receiving immune-modulating agents, who would be expected to have the same or greater risk of shingles as the proposed included conditions (systemic lupus erythematosus [SLE], polymyalgia rheumatica [PMR] and rheumatoid arthritis [RA]).

8.6.1. Members of the Dermatology Advisory Committee had noted the following studies:

- Chovatiya & Silverberg. J Am Acad Dermatol. 2021;85:1437-45
- Dreiher et al. J Eur Acad Dermatol Venereol. 2012;26:1127-32
- Wan et al. Br J Dermatol. 2022;186):664-72
- Wu et al. Dermatitis. 2023;34:241-9
- Traidl et al. Allergy. 2021;76:3017-27
- Bosma et al. J Eur Acad Dermatol Venereol. 2022;36:807-19.
- Rademaker et al. Australas J Dermatol. 2019;60:91-8

8.6.2. Members of the Dermatology Advisory Committee had proposed adding the following diseases to the list of planned for or treated with immune-modulating agents:

- atopic dermatitis
- psoriasis
- chronic discoid lupus erythematous (CDLE)
- bullous disorders (pemphigus and bullous pemphigoid)
- pyoderma gangrenosum
- mycosis fungoides
- dermatomyositis

8.6.3. Members of the Dermatology Advisory Committee had made the following relevant considerations:

8.6.3.1. Special consideration should be given to older age groups (>65 years) who require immunosuppressive treatments.

8.6.3.2. The risk of herpes zoster, and other viral infections, is high particularly in people with atopic dermatitis. People with atopic dermatitis often have more severe shingles than the people seen by rheumatology services. This is due to a combination of impaired local immunity and reduced barrier function of the skin, which is very different to non-dermatological conditions.

8.6.3.3. Key supporting evidence was provided by Chovatiya & Silverberg. J Am Acad Dermatol. 2021;85:1437-45, a cross-sectional observational study correlating shingles with chronic inflammatory skin disease in a representative cohort of US inpatient hospitalisations. In multivariate logistic regression models including age, sex, race/ethnicity, insurance, household income, and long-term systemic corticosteroid use, hospitalisation for shingles was highest for dermatomyositis (adjusted OR (aOR) 7.31 (95% CI 5.27-10.12), then pemphigus (4.78 (2.83-8.08)), then mycosis fungoides (3.79 (2.55-5.65), then atopic dermatitis (3.19

(1.93-5.28)). Other conditions with adjusted risks for shingles hospitalisation that were statistically significant were vitiligo (aOR 2.00), cutaneous lupus erythematosus (1.94), systemic sclerosis (1.92), bullous pemphigoid (1.77), sarcoidosis (1.52), and psoriasis (aOR 1.38 (1.14-1.68)).

8.6.3.3.1. The Committee noted Chovatiya & Silverberg study did not report on high-risk settings aside from people treated for chronic inflammatory skin diseases, eg haemopoietic stem cell transplantees. Members noted these other non-dermatological risk groups would have higher relative risks.

8.6.3.4. JAK inhibitors (e.g. upadacitinib) show an increased risk, such that dermatologists may routinely co-prescribe valaciclovir, as herpes zoster vaccine is not available to them.

8.6.3.5. Bullous pemphigoid, CDLE and pyoderma gangrenosum need long term, high doses of systemic corticosteroids, and increasingly need B-cell depletion therapy (e.g. rituximab).

8.6.3.6. People with severe dermatologic conditions are at significant risk of shingles because they receive immunosuppressive treatments for prolonged periods for severe inflammatory skin disease. The severe skin disease itself confers intrinsic increased risk of shingles even without extrinsic immunosuppression. Similar medicines are used to treat people with severe dermatologic diseases as in rheumatology. Immunosuppressive treatments use by dermatologists include ciclosporin, mycophenolate, methotrexate, azathioprine, and biologic agents. These treatments are often combined with prolonged high doses of prednisone, thereby compounding the potential risk.

8.6.3.7. Estimated numbers of people within the requested groups would include any dermatology patient where prednisone ≥20 mg/day will be continued for more than 4 weeks. Members noted the 4-week time period was expert opinion, rather than evidence based, but was consistent with the CDC definition of immunosuppression. People requiring two different immunomodulatory treatments (e.g. prednisone and methotrexate at the same time) would also be at increased risk. For atopic eczema, the potential population pool would be anyone with an EASI≥16, BSA≥10%, IGA≥3, but this could be restricted to people starting on a JAK inhibitor, or those that need more than one immune-modulating agent at the same time (e.g. methotrexate + prednisone, etc).

8.6.3.8. Members were unable to provide any evidence-based group size estimates for atopic dermatitis (which would be the biggest group), as it would depend on the special authority criteria for JAK inhibitors, should they be funded for atopic dermatitis. For the other dermatological conditions, there may perhaps 200 people.

8.6.3.9. Members estimated likely vaccine uptake in each group would depend on who was the treating clinician or service. If under dermatology specialty care, uptake would be high (>75%), if being treated by other specialties then possibly <50%.

8.7. The Committee noted consultation responses regarding other groups with conditions who are planning or receiving immune-modulating agents who would be expected to have the same or greater risk of shingles as the proposed conditions (SLE, PMR, RA):

- giant cell arteritis (GCA)

- psoriatic arthritis (PsA) on immune-modulating agents
- vasculitis on immune-modulating agents
- inflammatory bowel disease (IBD), including Crohn's disease
- multiple sclerosis (when treated with ocrelizumab and fingolimod).

8.8. The Committee noted the following features in the consultation responses:

8.8.1. People with GCA require a higher dose of prednisone (40 to 60 mg daily) compared when treating PMR (10 to 20 mg daily), conferring a much higher risk of developing shingles.

8.8.2. If people with IBD are treated with JAK inhibitors, they are considered to have at least the same risk of shingles as the proposed conditions.

8.8.3. People with multiple sclerosis may experience immunosuppression from the treatments they are receiving.

8.8.3.1. Treatment with ocrelizumab (449 people currently receiving) and fingolimod (348) are severely immunosuppressing.

8.8.3.2. By contrast, treatment with dimethyl fumarate (415 people currently receiving), natalizumab (562) and teriflunomide (50) are only mildly immunosuppressing.

8.8.4. Requests to add "People receiving high dose prednisone for prolonged periods" to the eligibility criteria, with respondents suggesting this could be defined as anyone receiving prednisone >10 mg daily for more than three months.

8.8.5. Requests to change the criterion "people living with poorly controlled HIV infection" to simply "people with HIV", noting that "poorly controlled" is a vague and undefined term that does not predict an immunological response.

8.8.5.1. The vaccine is expected to be most effective in those people with immunological recovery following initiation of antiviral therapy rather than those people with low CD4 cell counts for example. Consultation responses noted that there was evidence to support that people with HIV are expected to experience shingles more frequently than the general population.

8.9. The Committee considered it to would be more appropriate to amend the disease modifying anti-rheumatic drug (DMARD)-related criterion in its previous November 2023 recommendations for access criteria, by removing specific diseases and to instead take a risk-based approach that combines specified immune-modulating agents with dose, duration and patient age.

8.10. The Committee considered different immune-modulating agents to have different levels of risk for shingles. The Committee considered the most high-risk agents to be (in order) targeted synthetic agents eg JAK inhibitors, then biologic agents (monoclonal anti-TNF antibodies (eg. adalimumab, infliximab), B cell targeted therapies (eg. rituximab); then T cell co-stimulation modulators (abatacept), interleukin 6 (IL6) inhibitors (eg. tocilizumab), soluble TNF receptor fusion protein (eg. etanercept)), and lastly conventional synthetic immune-modulating agents (methotrexate, sulfasalazine, leflunomide, hydroxychloroquine).

8.10.1. The Committee noted again observational registry data for people with rheumatoid arthritis receiving biologic therapies in Germany 2007-2020, considered by the Committee in November 2023, where when adjusted for age, sex, corticosteroid usage, and indication, the relative risk of shingles was >3 times greater when receiving JAK inhibitors (adjusted hazard ratio (aHR) 3.66 (95% CI 2.38- 5.63) compared with conventional synthetic

DMARDs. Adjusted risks were also statistically significantly greater with monoclonal anti-TNF antibodies (aHR 1.63 (1.17-2.28) and B cell targeted therapy (1.57 (1.03-2.40) than conventional synthetic DMARDs. Central estimates in adjusted HRs for T cell co-stimulation modulators, IL6 inhibitors and soluble TNF receptor fusion protein were 1.45, 1.44 and 1.28 respectively, but with none reaching statistical significance (Redeker et al. Ann Rheum Dis. 2022;81:41-7).

8.11. The Committee considered the list of immune-modulating agents with dose, duration and patient age described in the eligibility criteria should elevate a person's risk of shingles to a level comparable or greater than that of people aged 65 years. The Committee indicated that this list with modifiers would be complex and require input from a variety of specialties. The Committee requested to review the compiled list at a future meeting.

8.12. The Committee considered that people planned for or who are receiving high-dose corticosteroid therapy for prolonged periods should be eligible for the recombinant zoster vaccine. The Committee considered the definition of high-dose corticosteroids in section 5.5.8 of the Immunisation Handbook relating to COVID-19 vaccines (which are non-live, and where recombinant zoster vaccine as an adjuvanted subunit vaccine is also non-live) for individuals with immunodeficiencies or receiving immunosuppressive agents individuals to be appropriate to define this group, ie. ≥20mg/day prednisolone-equivalent dose given for >10 days in the previous month.

8.13. The Committee noted its recommendations regarding the detail of the immune-modulating agent-related and corticosteroid-related criteria (criteria 2.f and 2.g) were provisional. Further work is to be done to specify the type of agents, daily doses, treatment durations, and age aspects as combined modifiers within those criteria for consideration at a future meeting.

8.14. The Committee noted that those aged over 65 years on immunomodulatory treatments have a particularly high risk of shingles, due to the combined effects of immunosenescence of age with immunocompromise from immunosuppressive treatments.

8.15. The Committee noted that funding of the herpes zoster vaccine for all people aged over 65 years (beyond those aged solely 65 years as currently funded) is currently listed on the Options For Investment list. The Committee reiterated that older age groups have a very high risk of shingles, at rates much higher than even those aged 65 years, and its strong view that the current eligibility criteria do not meet the highest health need.

9. Matters Arising: COVID-19 vaccine number of funded doses (Pharmac access criteria vs Te Whatu Ora guidance)

Recommendations

9.1. The Committee recommended that Pharmac amend the number of funded doses of Comirnaty Adult XBB.1.5 vaccine to align with the approved dose schedule in the supplier's data sheet.

Discussion

9.2. The Committee noted that since 1 July 2023, Pharmac has been responsible for the funding and management of COVID-19 vaccines in New Zealand, including managing their access criteria.

9.3. The Committee noted that in February 2024, Pharmac approved the release and distribution of Pfizer's Comirnaty Adult XBB.1.5 COVID-19 vaccine for use in New Zealand from 7 March 2024.

9.4. The Committee noted the approved dose schedule in the recently approved data sheet for Comirnaty Adult XBB.1.5 vaccine is a single dose regardless of prior vaccination status. It should be administered at least three months after the most recent dose of a COVID-19 vaccine.

9.5. The Committee noted that the data sheet for Comirnaty Adult XBB.1.5 vaccine does not distinguish between primary and booster doses. The approved dose schedule is the same regardless of previous vaccination status. It also states that additional doses may be administered to individuals who are severely immunocompromised, in accordance with official recommendations.

9.6. The Committee noted Health New Zealand – Te Whatu Ora (HNZ) has updated its clinical guidance to align with the data sheet dosing information, and now recommends a single dose of COVID-19 XBB 1.5 vaccine for those who are eligible aged 12 years and over, any additional dose is given after at least 6 months, regardless of number of previous COVID-19 vaccine doses received since the primary course.

9.7. The Committee considered that the number of funded Comirnaty XBB.1.5 doses should align with the Medsafe datasheet. The Committee noted Medsafe is currently assessing a regulatory application for Novavax's Nuvaxovid COVID-19 XBB.1.5 vaccine.

9.8. The Committee noted that the proposed populations and dosing schedule would be known once the vaccine has been approved.

10. RSVPreF3 vaccine for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus (RSV)

Application

10.1. The Advisory Committee reviewed the application for RSVPreF3 vaccine for the prevention of lower respiratory tract disease (LRTD).

10.2. The Advisory Committee took into account, where applicable, Pharmac's relevant decision-making framework when considering this agenda item.

Recommendation

10.3. The Advisory Committee recommended that the **RSVPreF3 vaccine for the prevention of RSV-LTRD for people aged 60 years and over** be **deferred**.

10.4. The Advisory Committee made this recommendation based on:

10.4.1. Insufficient evidence regarding the incidence of respiratory syncytial virus (RSV) in older people in New Zealand.

10.4.2. Uncertainty of the vaccine efficacy for people aged 80 years or for people aged 65 years and over who are immunosuppressed and or have unstable chronic medical conditions.

10.4.3. Uncertainty of the vaccine's duration of protection and when revaccination would be required.

Discussion

Māori impact

10.5. The Committee discussed the impact of funding RSVPreF3 vaccine for the prevention of RSV-LTRD on Māori health areas of focus and Māori health outcomes. The Committee noted one of Pharmac's Hauora Arotahi is Romaha Ora (respiratory health). The Committee considered respiratory illness, including RSV disease, across all ages among Māori to be a significant cause of inequitable health outcomes for Māori.

Impacts on Pacific peoples, disabled people, tāngata whaikaha Māori, and other people who have been underserved by the health system

10.6. The Committee discussed the impact of funding RSVPreF3 on Pacific peoples, disabled people, tāngata whaikaha Māori, and other people who have been underserved by the health system.

10.6.1. Members noted Pacific peoples are at greater risk of RSV-associated hospitalisation when compared to New Zealand European and other ethnicities (non-Māori).

10.6.2. Adults living in SES quintiles 3-5 were at higher risk of RSV-associated hospitalisation compared to adults living in SES quintile 1.

Background

10.7. The Committee noted respiratory syncytial virus (RSV) is highly infectious and transmitted between people through coughing, sneezing, sharing of saliva and/or by touching a contaminated surface. People usually have been infected with RSV before their second birthday. However, RSV infection does not provide durable or complete protection, so re-infection is common and can continue throughout life.

10.8. The Committee considered the impact on the individual from RSV to be comparable to influenza and other respiratory viruses. For most people RSV causes an upper respiratory tract infection and symptoms can include runny or blocked nose, cough, headache, fatigue and fever. Typically, people recover within one to two weeks.

10.9. The Committee noted RSV has the potential to cause a lower respiratory tract infection (LTRI) such as bronchitis, bronchiolitis and pneumonia. Common symptoms may include shortness of breath, weakness, fever, cough with or without sputum and fatigue. Severe disease requires hospitalisation, supplemental oxygen, intensive care or mechanical ventilation.

10.10. The Committee noted there are currently two vaccines for the prevention of RSV that have been licensed by the FDA and EMA: Arexvy (GSK) and Abrysvo (Pfizer). At the time of this meeting, no RSV vaccines had been Medsafe approved for New Zealand. The Committee noted Abrysvo (Pfizer) can be administered during late pregnancy and is associated with infants experiencing significantly reduced medically attended RSV-associated LTRD within 90 days of birth (6 infants of 3495 infants in the vaccine group vs 33/3480 in placebo group, vaccine efficacy 81.8% [99.5% CI 40.6-96.3%]) (Kampmann et al; MATISSE Study Group. N Engl J Med. 2023;388:1451-64).

10.11. The Committee noted palivizumab in children has been considered by various Advisory Committees in the past and was funded during the 2021, 2022 and 2023 RSV seasons to prevent severe RSV disease in babies at very high risk. For the 2022 and 2023 RSV seasons palivizumab was funded as part of the response to COVID-19 and its impacts, where in 2021 there was a pronounced rebound seasonal epidemic of RSV experienced internationally as a consequence of COVID-19 pandemic public health actions. Pharmac used the ring-fenced COVID-19 treatment budget to pay for palivuzmab, which was separate to the Combined Pharmaceutical

Budget. The separate funding for the COVID-19 response has now ended and palivuzmab is ranked on Pharmac's Options for Investment list. Committee members reiterated the importance that palivizumab, or a similar monoclonal antibody, be funded within the New Zealand Health care system for infants at high risk of RSV disease.

Health need

10.12. In New Zealand, RSV causes seasonal (winter) epidemics (similar to influenza) of acute respiratory tract infection experienced by people of all ages. (Farquharson et al. Public , Health. 2024:226:8-16).

10.13. The Committee noted the CDC NCIRD Surveillance Respiratory Virus Hospitalisation Surveillance Network which reports the burden of RSV through October to April each year in the USA and noted the greatest burden of RSV hospitalisation weekly incidence among people aged 65 years and over (≥65 years) was 6.1 per 100,000 people for 2023 and 9.5 per 100,000 for 2024. In comparison, the RSV hospitalisation weekly incidence rate among infants aged less than 1 year old was 179.6 per 100,000 for 2023 and 94.2 per 100,000 for 2024.

10.14. The Committee noted Staadegaard et al. Open Forum Infect Dis. 2021;8:ofab159, which pooled 15 countries' surveillance data from 2000 to 2020, and reported 55% of RSV cases were among children younger than 1 year old and 8% of cases among people aged 65 years and over.

10.15. The Committee considered that in New Zealand infants and children also experience a significantly larger burden of RSV disease compared to adults aged ≥65 years.

10.16. The Committee noted the CDC sentinel emergency department data from the USA which reported that of 64,074 people aged 65 and over (the peak of visits occurring the week ending 30 December 2023) who visited the participating emergency departments for respiratory illnesses, 6.3% were due to RSV, 58.4% COVID-19, and 35.2% influenza. The Committee considered COVID-19 and influenza to also be significant contributors to medically attended respiratory illness in older people in New Zealand.

10.17. The Committee noted surveillance data from the US CDC NCIRD Respiratory Virus Hospitalisation Surveillance Network reported a trending increase in the incidence of RSV hospitalisations among people aged ≥65 years following the COVID-19 pandemic.

10.18. The Committee noted that in early 2020, the COVID-19 public health measures New Zealand undertook were associated with a 98% reduction in RSV viruses detected in multiple surveillance systems in 2020 (versus the reference period of 2015–2019) (Huang et al. Nat Commun. 2021;12:1001).

10.19. The Committee noted Prasad et al. PloS One. 2020;15:e0234235, a retrospective observational study of the Southern Hemisphere Influenza and Vaccine Effectiveness Research and Surveillance (SHIVERS) data from 2012-2015 which included 4,600 people aged 18 years and over being admitted to hospital with an acute respiratory infection (ARI) who were tested for RSV. 348 people (7.6%) were identified to have RSV-associated ARI, the average length of stay was 4 days, 4 (1.1%) died during the hospital stay and 11 (3.2%) died within 30 days of hospital discharge and the average cost was $4,758 per event. There was no difference in risk factors between RSV and other respiratory infections. The Committee considered the presentation of RSV symptoms to be comparable to other respiratory infections.

10.19.1. The crude incidence rate was 44.7 (38.6-51.5) per 100,000 and when adjusted for non-testing was 99.2 (82.4-115.9) per 100,000 among people aged ≥65 years.

10.19.2. The Committee noted that when adjusted for age group and ethnicity, the associated risk of RSV associated hospitalisation in adults living in socioeconomic status (SES) quintiles 3-5 were at higher risk of RSV-associated hospitalisation compared to adults living in SES quintile 1.

10.19.3. The Committee noted that when adjusted for age group and SES, the associated risk of RSV associated hospitalisation among adults was higher among Māori (RR 2.8; 95% CI 2.0–4.0) and Pacific adults (RR 3.5; 95% CI 2.6–4.7) compared to those of European or other ethnicities.

10.19.4. The Committee considered the study to be an appropriate representation of New Zealand RSV hospitalisation cases.

- The data included severe acute respiratory infections (SARI) and non-SARI cases.
- The winter surveillance included 89.5% of RSV hospitalisations, and so therefore is a suitable estimate for annual incidence.
- The Committee considered overnight admissions, as used in the manuscript, to be the best-defined descriptive measure for hospital morbidity in New Zealand. Alternative definitions, such as “admitted to hospital” including emergency departments stays longer than 3 hours over-estimates true admission rate and hospital resource use.

10.20. The Committee noted Prasad et al. Clin Infect Dis. 2021;73:e158-e163, a retrospective observational study using SHIVERS data to estimate the relative risks of RSV hospitalisation in adults (18-80 years) posed by chronic medical conditions. The Committee noted that of the 281 RSV-associated ARI, 81% had a chronic medical condition. The most common conditions were asthma (61.6%), chronic obstructive pulmonary disease (COPD) (48.8%) and diabetes mellitus (32.7%). The Committee considered these comorbidities to be well-established risks for RSV in older adults.

10.21. The Committee noted Farquharson et al. Public , Health. 2024:226:8-16 reported that there is no robust community RSV prevalence data published for people aged 60 years and over for New Zealand or Australia. The Committee considered local data is vital for robust estimates, as RSV epidemiology varies by country and latitude.

10.22. The Committee noted that statistical adjustments are used in RSV studies to correct for under-ascertainment of cases.

10.23. The Committee noted Onwuchekwa et al. J Infect Dis. 2023;22:173-184, a systematic review and metanalysis which included 154 studies over 2000-21. The Committee noted that compared to real-time reverse transcriptase polymerase chain reaction (RT-PCR), other RSV detection methods were less sensitive. Compared to singleplex RT-PCR, multiplex RT-PCR is less sensitive. Two specimen tests with RT-PCR were more sensitive compared to a single nasal/nasopharyngeal swab.

10.24. The Committee noted McLaughlin et al. Open Forum Infect Dis. 2022;9:ofac300, a systematic review and metanalysis which included 14 studies of medically attended RSV cases among adults. The pooled annual incidence rate was 178 per 100,000 people (95% CI 152–204; n=8 estimates) hospitalisations among people aged ≥65 years, 133 per 100,000 people (95% CI 0–319; n=2) emergency department presentations and 1519 per 100,000 people (95% CI 1109–1929; n=3) outpatient visits. Following adjustment for under-ascertainment the incidence rates were 267 per 100,000 people for hospitalisations (uncertainty interval [UI], 228–306), 200 per 100,000 people for emergency department presentations (UI, 0–478) and 2278 per 100,000 people for outpatient visits (UI, 1663–2893). People with co-morbidities had a 1.2-28 times greater risk to be hospitalised with RSV compared to people without.

10.25. The Committee noted Savic et al. Influenza Other Respir Viruses. 2023 ;17:e13031, a systematic literature review and metanalysis which included 21 studies estimating the burden of RSV among people aged ≥60 years in high-income countries over 2000-2022. The pooled estimates were 1.62% (95% CI 0.84-3.08) for RSV-ARI, 0.15% (95% CI 0.09-0.22) for hospitalisations in whom 7.13% (95% CI 5.40-9.36) died.

10.26. The Committee noted Li et al. Lancet. 2022;399:2047-2064, a systematic review and modelling study. When adjusted for under-ascertainment the incidence rate was 347 per 100,000 (95% CI 203-595) for hospitalisations in people aged ≥65 years.

10.27. The Committee considered there is a health need to prevent/treat RSV for people aged ≥65 years. The Committee considered the evidence to be of high strength, moderate quality regarding the incidence of severe disease. The Committee considered the evidence less applicable to New Zealand, as hospitalisation and mortality incidence rates are lower for New Zealand compared to estimates from other international studies. The Committee considered there is currently insufficient high-quality epidemiological data to understand the health need of RSV in older New Zealanders.

10.28. The Committee noted the applicant's estimate of symptomatic RSV infection among people aged ≥60 years to be 5.83/100 person-years (range 5.58-8.48). The Committee noted the estimate was derived from a meta-analysis completed by the supplier that included three international studies: Falsey et al. N Engl J Med. 2005;352:1749-59, Korsten et al Eur Respir J. 2021;57:2002688 and Pērez et al. Open Forum Infect Dis. 2023;10:ofad111. The Committee considered the metanalysis was suboptimal for the following reasons:

10.28.1. Only a small number of the international studies reporting incidence were included in the metanalysis.

10.28.2. The metanalysis needed to be adjusted for detection techniques: multiplexing RT-PCR, serology ≥4-fold seroconversion and the type of specimen(s) collected. The metanalysis included papers with collection and laboratory techniques that were up to two decades old.

10.28.3. The metanalysis did not report a risk of bias assessment, which the Committee considered a significant limitation of the reporting.

10.28.4. The Committee noted the model uses a seasonality adjustment of 0.67 derived from Australian data. The Committee considered this to be inappropriate due to these studies being conducted in the Northern hemisphere and the higher latitude tends to have a shorter more defined RSV season. The Committee considered the Prasad et al. PloS One. 2020;15:e0234235 reported an appropriate estimation of hospitalisation rates for New Zealand.

10.29. The Committee considered family and whānau of people with RSV-associated LRTD would need to take time off paid work to care for the person if they are bed bound and/or hospitalised. The Committee considered it to be appropriate to use data from New Zealand influenza studies to inform the economic assessment.

10.30. The Committee noted Pharmac's Hauora Arotahi (Māori health areas of focus) identifies 'respiratory health' (Romaha Ora) among the five health areas of focus for Māori. It has been previously noted that Māori are at greater risk of RSV-associated hospitalisation when compared to New Zealand European and other ethnicities (non-Pacific peoples) (Prasad et al. 2020). The Committee considered respiratory illness including RSV disease across all ages among Māori to be a significant cause of inequitable health outcomes for Māori.

10.31. The Committee considered Pacific peoples to be at greater risk of RSV-associated hospitalisation when compared to New Zealand European and other ethnicities (non-Māori), and adults living in SES quintiles 3-5 were at higher risk of RSV-associated hospitalisation compared to adults living in SES quintile 1 (Prasad et al. 2020).

Health benefit

10.32. The Committee noted RSVPreF3 is an adjuvanted vaccine containing the antigen Respiratory Syncytial Virus recombinant glycoprotein F stabilised in the pre-fusion conformation (RSVPreF3). This induces a CD4 T cell response against RSV glycoprotein F.

10.33. The Committee noted RSVPreF has been assessed in the AreSVi-006, 004 and 007 trials.

10.34. The Committee noted the AreSVi-006 study is an ongoing, randomised, placebo-controlled, multi-country, phase three trial in 24,965 people aged ≥60 years with stable chronic medical conditions. People were excluded if they were undergoing immunosuppression, had unstable chronic medical conditions, were bedridden or considered to have a survival length of less than 3 years. The Committee considered the excluded populations representative of a large proportion of people living in aged-care facilities in New Zealand.

10.34.1. The Committee noted Papi et al. N Engl J Med. 2023;388:595-608 that reported results of the AreSVi-006 study over one RSV season (median follow-up 6.7 months).

- In the vaccine group there were 7 RT-PCR confirmed cases of RSV associated lower tract respiratory infection (LTRI) compared to 40 cases in the placebo group, the vaccine efficacy against RSV-LTRI was 82.6% (95% CI 57.9-94.1).
- In the vaccine group there were 27 RT-PCR confirmed cases of RSV associated ARI and 95 cases in the placebo group, the vaccine efficacy against RSV-ARI was 71.7% (95% CI 56.2-82.3).
- In the vaccine group there were 1 RT-PCR confirmed case of severe RSV associated LTRI (determined by the investigators) and 17 in the placebo group, the vaccine efficacy against severe RSV-LTRI was 94.1% (95% CI 62.4-99.9).
- Most adverse events were mild to moderate and resolved within four days. The Committee noted 11 (0.09%) people reported atrial fibrillation within 30 days in the vaccine group compared to 4 (0.03%) in the placebo group, these numbers were similar at 6 months post vaccine.
- There were 4 people with RSV who required oxygen, 2 who required hospitalisation and there were no deaths.
- The Committee noted no conclusions regarding vaccine efficacy could be made for people aged ≥ 80 years.
- The Committee considered this study had the following limitations:
    - The study was affected by the COVID-19 pandemic, which resulted in some public health measures in some countries reducing RSV incidence as well as altering the RSV season.
    - The study was not statistically powered to analyse hospitalisations or deaths. The benefit is shown only against RSV RT-PCR endpoints.

- The trial population was healthier than those that are at the greatest risk of RSV disease.

10.34.2. The Committee noted Feldmen et al. Clin Infect Dis. 2024; 78:202-209, which reported a secondary analysis of the results of the AreSVi-006 study over one season.

- Approximately 39% had ≥1 condition of interest. Efficacy against RSV-LRTD was high in participants with ≥1 condition of interest (94.6%), ≥1 cardiorespiratory (92.1%), ≥1 endocrine/ metabolic (100%), and ≥2 conditions of interest (92.0%). Efficacy against RSV-ARI was 81.0% in participants with ≥1 condition of interest (88.1% for cardiorespiratory, 79.4% for endocrine/metabolic conditions) and 88.0% in participants with ≥2 conditions of interest.
- The Committee considered the vaccine efficacy to be comparable between people with and without the conditions of interest.

10.34.3. The Committee noted Ison et al. Clin Infect Dis. 2024 :ciae010, which reported results of the AreSVi-006 study over two RSV seasons (median follow-up 17.8 months).

- In the second season, people who received the vaccine were randomised to receive another dose of the vaccine or placebo.
- In the single dose vaccine group, there were 30 RT-PCR confirmed cases of RSV associated lower tract respiratory infection (LTRI) compared to 139 cases in the placebo group, the vaccine efficacy against RSV-LTRI was 67.2% (97.5% CI 48.2–80.0%). In the revaccination group there were also 30 cases the vaccine efficacy against RSV-LTRI was 67.1% (97.5% CI 48.1-80.0%).
- In the single dose vaccine group, there were 94 RT-PCR confirmed cases of RSV associated ARI compared to 292 cases in the placebo group, the vaccine efficacy against RSV-ARI was 52.7% (95% CI 40.0-63.0). In the revaccination group there were 80 cases, the vaccine efficacy against RSV-ARI was 60.3% (95% CI 48.8-69.5).
- In the single dose vaccine group, there were 7 RT-PCR confirmed events of severe RSV- LTRI compared to 48 events in the placebo group, the vaccine efficacy against RSV-LTRI was 78.8% (95% CI 52.6-92.0). In the revaccination group there were 7 confirmed cases the vaccine efficacy was 78.8% (95% CI 52.5- 92.0).
- In the single dose vaccine group, there were 12 medically attended RSV-LTRI events compared to 63 in the placebo group, the vaccine efficacy against medically attended RSV-LTRI was 73.1% (95% CI 49.4-86.9).
- In the single dose vaccine group, there were 32 medically attended RSV-ARI events compared with 94 in the placebo group, the vaccine efficacy against medically attended RSV-ARI was 52% (95% CI 27.3-69.1).
- Most adverse events were mild to moderate and resolved within four days.
- Atrial fibrillation occurred for 3 (0.06%) in the revaccination group compared with 5 (0.05%) in the placebo group, thirty days post second

vaccination and 11 (0.22%) in the revaccinated group and 13 (0.13%) in the placebo group, 6 months post dose 2.

- The Committee noted there is waning in the vaccine efficacy following one year and that revaccination did not provide additional protection against any kind of RSV related outcome. The Committee considered it to not be appropriate to revaccinate people after one year.

10.35. The Committee noted the AreSVi-007 study, randomised, placebo-controlled, multi-country, phase three trial including 885 people aged ≥60 years, with the same inclusion and exclusion criteria as the AreSVi-006 trial.

10.35.1. The Committee noted Chandler et al. Clin Infect Dis. 2024:ciad786, which reported the results of the trial, where the RSVpreF vaccine was either co-administered (Co-Ad) with the FLU-QIV vaccine or with FLU-WIV administered 31 days following (SA).

- RSV-A neutralisation titres in the co-administration group were noninferior compared with the sequential administration group. The GMT ratio was 1.27 (95% CI 1.12–1.44) between the SA and Co-Ad groups 1-month post-RSVPreF3 OA vaccination (day 31 for Co-Ad group and day 62 for SA group).
- The HI titres for each of the FLU vaccine strains in the Co-Ad group were noninferior compared with the SA group. The GMT ratio of FLU A/H3N2, FLU A/H1N1, FLU B/Yamagata, and FLU B/Victoria strains (1/DIL) was 1.17 (95% CI 1.02–1.35), 1.22 (95% CI 1.03–1.44), 1.17 (95% CI 1.04–1.32), and 1.10 (95% CI 0.95–1.26) between the SA and Co-Ad groups, respectively.
- Most adverse events were mild to moderate and there was a low frequency of grade 3 events.
- The Committee noted non-inferiority was met however in the co-administration group all titres were numerically lower. The Committee considered the clinical significance of this is uncertain.

10.36. The Committee noted there were three cases of inflammatory neurological events across all AreSVi trials, there was one case of Guillain- Barré syndrome and two cases of acute disseminated encephalomyelitis (in both cases, the RSV vaccine was co-administered with the influenza vaccine and diagnosis was only by clinical assessment).

10.37. The Committee considered the health benefits of RSVPreF to be a reduction in RSV-associated: ARI, LTRI, and LTRI medical visits. The Committee considered there to be insufficient evidence regarding the vaccine efficacy in preventing RSV hospitalisations. The Committee considered the vaccine to have a suitable safety and reactogenicity profile. The Committee considered the safety signal regarding atrial fibrillation to be of uncertain importance.

10.38. The Committee considered people with stable medical conditions between the ages of 60 to 79 years would benefit most from RSVPreF3 but there is uncertainty regarding the vaccine's efficacy in people aged ≥ 80 years.

10.39. The Committee considered that there is clear evidence that revaccination at one year after the initial vaccination is unnecessary, but there is evidence of waning in vaccine efficacy with time. The Committee considered the rate of vaccine waning to be uncertain. The Committee considered there to be insufficient evidence supporting a three-yearly vaccination schedule and it is not clear when revaccination should be considered. Moreover, there is uncertainty in those individuals with 'unstable' chronic

disease and in people with a life expectancy of ≤ 3 years, who would be at high-risk for RSV disease consequences.

10.40. The Committee considered that family and whānau would experience health benefit as they would not be having to care for or transport to medical visits their elderly relatives with RSV, and their health benefit would be comparable to that used in models used for influenza vaccination.

10.41. The Committee considered there to be insufficient evidence that RSV immunisation of the elderly would confer protection for infants against acute bronchiolitis. The Committee considered it more likely that immunisation of infants would confer protection for the elderly, similar to the epidemiology of influenza vaccination.

Suitability

10.42. The Committee considered the non-clinical features of the vaccine to be the need to reconstitute the vaccine and store refrigerated for up to a maximum of 4 hours (following reconstitution). While problematic, the Committee considered these features to be comparable to some vaccines currently available.

10.43. The Committee considered it to be ideal for an RSV vaccine to be administered at the same time as the seasonal influenza and SARS-CoV-2 vaccine. The Committee considered that the influenza vaccine could be administered with the RSVPreF vaccine, however the safety with other vaccines, including SARS-CoV2 is unknown.

Cost and savings

10.44. The Committee considered there would be no significant changes in health-sector expenditure other than for direct treatment costs. Sector costs would depend on whether RSVPreF was co-administered with seasonal influenza and/or SARS-CoV-2 vaccine instead of at an additional vaccination event.

10.45. The Committee considered the expected RSVPreF3 vaccine uptake initially to be slightly lower than that of the influenza vaccine, even if co-administered, as there is likely to be some confusion particularly regarding the understanding of RSV as an illness in adults, but potentially also the perception that co-administration may result in worse adverse events.

10.46. The Committee considered there was significant uncertainty around the supplier's modelling that the vaccine would be administered every three years and noted that this was likely to be a key assumption in economic modelling.

10.47. The Committee considered that the supplier Cost-Utility Analysis (CUA) was appropriately structured to capture the potential costs and health benefits from the RSVPreF3 vaccine.

10.48. The Committee considered that the assumptions included in the supplier CUA were different to others in the literature and would likely need to be adapted for the New Zealand context.

10.48.1. The RSV incidence should be informed by the placebo arm in Papi et al. N Engl J Med. 2023 (1.39 per 100 person years), with sensitivity analysis informed by other studies such as Li et al. Lancet. 2022 and Savic et al. Influenza Other Respir Viruses. 2023. These studies all reported lower incidence than in the supplier model, which was 5.83 per 100 person years.

10.48.2. Assumptions around hospitalisation and death should be informed by New Zealand evidence, where possible, such as Prasad et al. 2020. Studies were not powered to assess the vaccine efficacy in preventing hospitalisation or death.

10.48.3. The vaccine efficacy waning assumptions used by the supplier were conservative, meaning that the efficacy may plausibly last longer than the supplier had forecast.

Summary for assessment

10.49. The Advisory Committee considered that the table below summarises its interpretation of the most appropriate PICO (population, intervention, comparator, outcomes) information for the RSVPreF3 vaccine if it were to be funded in New Zealand for the prevention of LRTD caused by RSV. This PICO captures key clinical aspects of the proposal and may be used to frame any future economic assessment by Pharmac staff. This PICO is based on the Advisory Committee's assessment at this time and may differ from that requested by the applicant. The PICO may change based on new information, additional clinical advice, or further analysis by Pharmac staff.

Population	Adults aged ≥ 60 years The supplier has also provided detail on subpopulations of interest: - Adults ≥ 65 years of age - Adults ≥ 75 years of age - Māori and Pacific ≥ 60 years of age Other high-risk subpopulations (aged ≥ 60 years with comorbidities, aged ≥ 75 years with comorbidities, aged ≥ 60 years living in a long-term care facility (LTCF)
Intervention	0.5mL RSVPreF vaccine administered via intramuscular injection (Duration of vaccine cycle TBC). Can be co-administered with the influenza vaccine.
Comparator(s)	No vaccination
Outcome(s)	Reduced likelihood of: - RSV-related LRTD. In the overall group from the AresVi-006 (Papi et al. N Engl J Med. 2023;388:595-608) trial, VE was 82.6% over one RSV season - RSV-related ARI. In the overall group from AreSVi-006, VE was 71.7% over one RSV season. Resulting in: - Improved health-related quality of life (HRQoL) There may be some health system savings and capacity relief from reduced inpatient and outpatient events, however evidence to date does not support a reduction in RSV-related mortality or hospitalisations.
Table definitions: Population, the target population for the pharmaceutical; Intervention, details of the intervention pharmaceutical; Comparator, details the therapy(s) that the patient population would receive currently (status quo – including best supportive care); Outcomes, details the key therapeutic outcome(s) and source of outcome data.	

11. COVID-19 vaccine clinical applications

Application

11.1. The Committee noted that Pharmac is now responsible for the management of COVID-19 vaccines, following a transfer of responsibilities from Ministry of Health in July 2023. Pharmac is planning to run a competitive procurement process for the supply of COVID-19 vaccines for eligible populations in late 2024.

11.2. The Committee noted that Pharmac staff sought clinical advice from the Committee to inform Pharmac's understanding of vaccine technologies platforms, the different populations in New Zealand who may need access to them and how changes to the COVID-19 vaccines available in New Zealand could be managed.

11.3. The Committee noted that the purpose of seeking this advice was to enable Pharmac to scope a competitive procurement activity for COVID-19 vaccines in New Zealand and to identify any issues that would need to be considered during this process.

11.4. The Committee noted that in August 2023, Pharmac released a call for applications from pharmaceutical suppliers who manufacture vaccines against COVID-19 in order to understand more about potential vaccine candidates and inform any future procurement process. The call for applications was open to all suppliers and technology platforms and four applications were received from four suppliers, involving vaccines with RNA or protein-based technologies.

11.5. The Committee noted that any procurement process for COVID-19 vaccines undertaken by Pharmac may include proposals for vaccines or technology platforms not considered at this meeting and that further clinical advice may be needed throughout this process.

11.6. The Advisory Committee noted applications were received for the following four COVID-19 vaccines, whose health benefits and suitability the Committee considered separately for each. These applications were for:

11.6.1. elasomeran, elasomeran and davesomeran, andusomeran vaccine (Spikevax – Moderna)

11.6.2. SARS-CoV-2 rS XBB1.5 vaccine (Nuvaxovid XBB1.5 – Novavax)

11.6.3. tozinameran, riltozinameran, famtozinameran, raxtozinameran (BNT162b2) vaccine (Comirnaty –Pfizer)

11.6.4. ARCT-154 vaccine (CSL-Seqirus)

11.7. The Advisory Committee took into account, where applicable, Pharmac's relevant decision-making framework when considering this agenda item, including for each of the COVID-19 vaccines considered.

11.8. The Committee provided advice but made no recommendations on the funding of the applications received nor on procurement activities.

Discussion

Māori impact

11.9. The Committee discussed the impact of funding COVID-19 vaccines for the prevention of COVID-19 infection on Māori health areas of focus and Māori health outcomes. The Committee noted its previous considerations from November 2023 that Māori have higher age-standardised rates of hospitalisation and mortality associated with COVID-19, compared to people of New Zealand European/other ethnicity, and should be prioritised for continued vaccination. The Committee noted that vaccines, immunisation and infectious diseases including COVID-19 are not a part of Pharmac's Hauora Arotahi (Māori health areas of focus).

Impact on Pacific peoples, disabled people, tāngata whaikaha Māori, and other people who have been underserved by the health system

11.10. The Committee noted its previous considerations from its November 2023 meeting of the impact of funding COVID-19 vaccines for the prevention of COVID-19 infection on people who have been underserved by the health system. The Committee noted that Pacific peoples have higher age- standardised rates of hospitalisation and mortality associated with COVID-19, compared to people of New Zealand European/other ethnicity, and considered they should be prioritised for future eligibility for vaccination.

11.11. The Committee considered that people receiving Disability Support Services (DSS) funding comprise a vulnerable, high needs group of people with varying intellectual or physical disabilities. The Committee considered that the data for the risks of hospitalisation and mortality from the general population were not generalisable to all disabled people in New Zealand. The Committee considered that disabled people were an important group to prioritise for future eligibility for vaccination.

Background

11.12. The Committee noted it's previous consideration for the use of XBB.1.5 variant vaccines in New Zealand in October 2023 and previous consideration of the eligibility criteria for funding of booster vaccinations in November 2023.

Moderna: **elasomeran, elasomeran and davesomeran, andusomeran vaccine (Spikevax) for the prevention of COVID-19**

Health benefit

11.13. The Committee noted that the elasomeran, elasomeran and davesomeran, andusomeran vaccine uses the mRNA platform.

11.14. The Committee noted that the application included three COVID-19 variant formulations in three populations (children 6 months to 11 years, adolescents 12 to 17 years and adults 18 years and over):

11.14.1. Monovalent original wild-type vaccine (Spikevax)

11.14.2. Bivalent original wildtype and Omicron BA.4/5 vaccine (Spikevax bivalent)

11.14.3. Monovalent Omicron XBB.1.5 vaccine (Spikevax XBB.1.5)

11.15. The Committee noted a phase 3 randomised, observer blinded, placebo-controlled trial of the original wild-type vaccine assessing the efficacy of the vaccine in prevention of symptomatic SARS-CoV-2 infection up to 120 days including 30,415 participants 18 years and over. The Committee noted that the vaccine efficacy was reported as 94.1% for the prevention of symptomatic SARS-CoV-2 infection. The Committee noted that injection site reactions were more common with vaccine treated participants compared to placebo, but rates of medically attended and serious adverse events were similar across both groups (Baden et al. N Engl J Med 2021;384:403-16). The Committee noted that this was the pivotal trial for the use of vaccine for those over 18 years old. The Committee noted that the data for follow up to day 240 was also included in the application (El Sahly et al. N Engl J Med 2021; 385:1774-85). The Committee noted that the reported vaccine efficacy for the prevention of symptomatic SARS-CoV-2 from this trial was 93.2%, and 98.2% for the prevention of severe disease. The Committee considered that the safety profile of the vaccine was similar to that observed in the previously published results (Baden et al. 2021).

11.16. The Committee noted a phase 2/3, placebo-controlled trial of healthy adolescents aged 12 to 17 years in the United States. The Committee noted that this study assessed the non-inferiority of the immunogenicity of the vaccine in those 12-17 years compared to those 18 years and over (Ali et al. N Engl J Med 2021; 385:2241-51). The Committee noted the reported vaccine efficacy was 93.3% for the prevention of symptomatic SARS-CoV-2 infection. The Committee noted that the case definition for symptomatic SARS-CoV-2 infection was amended from the per-protocol definition due to the low numbers of cases. The Committee considered that the safety profile of the vaccine in 12- to 17-year-olds was similar to other trials described above.

11.17. The Committee noted a phase 2-3 trial that was open label for dose selection (part 1) and observer-blinded, placebo-controlled expansion evaluation of the selected dose

(part 2) in the USA and Canada. The Committee noted that the study population was children aged 6 to 11 years. The Committee noted that the primary objectives were to assess the safety of the vaccine in children and the non-inferiority of immune response compared to young adults (18 to 25 years of age) (Creech et al. N Engl J Med 2022; 386:2011-23). The Committee noted the vaccine efficacy for the prevention of symptomatic SARS-CoV-2 infection was 74.0% to 91.8% depending on the case definition. The Committee noted that the per-protocol case definition was more restrictive and case numbers were lower compared to case numbers using other definitions. The Committee noted that the other definitions used were CDC definition or the COVE adult trial definition. The Committee noted that it was reported that the immunogenicity results were non-inferiority compared to young adults. The Committee considered that the safety profile in children 6 to 11 years was similar to the other trials described above.

11.18. The Committee noted a phase 2-3 trial that was open label for dose selection (part 1) and observer-blinded, placebo-controlled expansion evaluation of the selected dose (part 2) in children 6 months to 5 years. The Committee noted the primary objectives were to assess the reactogenicity of the vaccine, and noninferiority of immune response compared to young adults (18 to 25 years) in a related trial (Anderson et al. N Engl J Med 2022; 387:1673-87). The Committee noted that the trial demonstrated non-inferiority of immunogenicity in people aged 6 months to 5 years when compared to young adults.

11.19. The Committee considered that evidence from vaccine safety monitoring systems globally supports a causal association between mRNA COVID-19 vaccines and increased risk of myocarditis and pericarditis. The Committee noted the overall incidence of myocarditis and pericarditis is reported as 0.95 per 100,000 doses. The risk of myocarditis and pericarditis was higher in younger men 18-24 years of age who had receive two doses of the vaccine. The Committee noted that some studies reported a slightly higher risk of myocarditis and pericarditis with mRNA-1273 (Spikevax) compared with BNT162b2 mRNA (Comirnaty) (Heidecker et al. Eur J Heart Failure 2022; doi:10.1002/ejhf.2669).

11.20. The Committee noted that the pivotal trials were conducted in earlier variant eras (most in Delta or the beginning of Omicron variant circulation) and that the participants were likely COVID-19 naïve. The Committee considered that in the current New Zealand context the trial data was less useful as most people have had exposure to COVID-19 vaccination and/or COVID-19 infection. The Committee considered that the data for booster doses (including XBB.1.5) would be most useful as New Zealand is currently transitioning to using XBB.1.5 variant vaccines.

11.21. The Committee noted a focus of the application on comparison with the currently funded mRNA vaccine. The Committee noted that a retrospective cohort study including over 6 million older US adults assessing comparative risks of adverse events between Comirnaty and Spikevax vaccines (Harris et al. JAMA Network Open. 2023;6:e2326852). The Committee considered that overall the data reflects similar vaccine efficacy and safety profiles.

11.22. The Committee noted a Cochrane systematic review assessing the efficacy and safety of COVID-19 vaccines (Graña et al. Cochrane Database of Systematic Reviews. 2022;12). The Committee noted the high certainty of evidence for outcomes of confirmed symptomatic COVID-19, severe or critical COVID-19, and serious adverse events. The Committee noted the moderate certainty of evidence for confirmed SARS-CoV-2 infection.

11.23. The Committee noted authorisations from international agencies for Spikevax XBB.1.5:

11.23.1. Food and Drug Administration: approved in September 2023 for people 12 years and over.

11.23.2. European Medicines Agency: approved in September 2023 for people aged 6 years and over.

11.23.3. Therapeutic Goods Administration: approved in October 2023 for people aged 12 years and over.

Suitability

11.24. The Committee noted that the vaccine would be supplied in multidose vials for children's vaccination. The Committee considered that multidose vials increase wastage on children's vaccination due to the small number of children vaccinated on any day. The Committee considered that pre-filled syringes are preferred but the additional packaging often requires more storage space.

Novavax: **SARS-CoV-2 rS XBB1.5 vaccine (Nuvaxovid XBB1.5) for the prevention of COVID-19**

Health benefit

11.25. The Committee noted that the application from the supplier considered the use of SARS-CoV-2 rS XBB.1.5 variant vaccine (Nuvaxovid XBB.1.5) for active immunisation against COVID-19, to help inform future procurement processes for COVID-19 vaccines.

11.26. The Committee noted that Nuvaxovid XBB.1.5 is an adjuvanted vaccine composed of purified full-length SARS-CoV-2 recombinant spike (S) protein stabilised in its prefusion conformation and a saponin-based Matrix-M adjuvant to enhance the S protein-specific immune response. The Committee noted that this adjuvant is also used in other vaccines.

11.27. The Committee noted that the dosing of Nuvaxovid (original, wild-type vaccine) was recommended as a primary series of two doses 3 weeks apart and booster 6 months after primary series in individuals 18 years and over. The Committee noted that the use of the Nuvaxovid XBB.1.5 vaccine is currently under Medsafe evaluation as a booster for people 12 years of age and over.

11.28. The Committee noted that the Food and Drug Administration (FDA) approved Nuvaxovid XBB.1.5 vaccine in October 2023. The Committee noted that the European Medicines Agency (EMA) had approved Nuvaxovid XBB.1.5 vaccine in October 2023. The Committee noted that at the time of this meeting that the Therapeutic Goods Administration (TGA) Australia was still evaluating Nuvaxovid XBB.1.5 vaccine.

11.29. The Committee considered that there is a large body of evidence assessing Nuvaxovid against placebo in the primary series, and a smaller body of evidence comparing Nuvaxovid to Comirnaty, and as a booster dose.

11.30. The Committee noted studies 301 and 302 were the randomised control trials that provided the efficacy data for use of Nuvaxovid for primary series of vaccination in people 18 years and over (Heath et al. N Engl J Med 2021; 385:1172-1183; Dunkle et al. N Engl J Med 2022; 386:531-43 and Marchese et al. Vaccine. 2023; 41: 3461–66). The Committee noted the vaccine efficacy against mild, moderate and severe disease in older adults (65-84 years) was reported to be 90% across two clinical trials (Heath et al. 2021and Dunkle et al. 2022). The Committee noted that in adolescents aged 12 to 17 years efficacy against symptomatic infection was reported as 79.5% (95% CI, 46.8%-92.1%) after the primary series (Anez et al. JAMA Netw Open.2023;6:e239135). The Committee noted that there were no severe cases of

disease reported in participants receiving Nuvaxovid, yielding a vaccine efficacy against severe disease of 100% (95% CI, 87.0 to 100) and against hospitalisation of 100% (95% CI, 28.8-100) (Marchese et al. 2023).

11.31. The Commitee noted that only immunogenicity data was available for booster doses. The Committee noted that the reported increase in geometric mean neutralising antibody titres was approximately four-fold higher than after the primary series, in participants aged 18 to 84 years (Mallory et al. Lancet Infect Dis 2022; 22: 1565–76).

11.32. The Committee considered that the protective threshold for neutralising antibody titres against COVID-19 was unclear because the studies reporting associations between neutralisation titres and vaccine efficacy used various methods, data sources (various clinical trials) and different assays to assess neutralisation.

11.33. The Committee noted a study that assessed neutralising antibody titres as correlates of protection against COVID-19 from Study 301, suggested that the geometric mean neutralising antibody titres following a third dose correlated with vaccine efficacy estimate of over 80% in the entire study cohort and in those 60-84 years (Fong et al. Nat Microbiol. 2022;7:1996-2010). The Committee considered that applying the estimated correlates of protection from immunogeniticity data for Nuvaxovid would correspond to an efficacy against Omicron BA.1 and BA.5 variants of 65% to 95%, depending on which study informed the correlate of protection. The Committee considered however, that a key limitation of these estimates was that they were based on correlates of protection against the ancestral variant of SARS-CoV-2, and that the correlation between geometric neutralising antibody titres and vaccine efficacy may differ for the currently circulating variants.

11.34. The Committee noted the COV-BOOST clinical trials that evaluated multiple vaccine technologies including a comparison of Nuvaxovid and Comirnaty (Pfizer) original vaccines (Liu et al. J Infect. 2022;84:795–813 and Liu et al. J Infect. 2023;87:18-26). The Committee noted that the three trials included reported that the immune response for Nuvaxovid was comparable to Comirnaty in people aged 12 years and over. The Committee considered that this data also suggests that Nuvaxovid provides long lasting responses, up to eight months post vaccination. The Committee noted that the COV-BOOST study also reported that participants who received Nuvaxovid as a booster dose had a slower decay rate than those who received Comirnaty as a booster dose. The Committee noted that other studies supplied were Com-COV-2 (Shaw et al. J Infect. 2023; 86: 574–83; Stuart et al. Lancet 2022; 399: 36–49) and Com-COV-3 (Kelly et al. J Infect. 2023 [Epub ahead of print]).

11.35. The Committee noted the supplied evidence relating to the Nuvaxovid XBB.1.5 variant vaccine including unpublished data. The Committee noted data from study 313 (unpublished) that evaluated seroresponse rates compared to the original vaccine. The Committee noted that there were two groups, those who had received an mRNA vaccine and those who are unvaccinated but had history of infection. The Committee noted that the reported seroresponse from the XBB.1.5 is non-inferior compared to the original vaccine. The Committee noted that there were higher levels of neutralising antibody titres (geometric mean titre ratio: 5.8 (95% CI, 4.85 to 6.91)) and seroconversion rates (difference in seroconversion rates: 57.2 (95% CI, 50.5 to 63.2)) for XBB.1.5 variant compared to the historical Nuvaxovid vaccinated control from a previous study. The Committee noted that of the treatment groups, 66.9% receiving the original vaccine, compared to 56.9% the XBB.1.5 vaccine reported local reactions including injection site reactions and 47.6% compared to 55.4% reported systemic reactions. The Committee noted a study in mice and non-human primates that reported cross-neutralising antibodies to other variants (Omicron XBB lineages subvariants) and that the XBB.1.5 vaccine provides an immune response regardless of previous vaccination with other variant vaccines (Patel et al. Sci Rep.

2023;13:19176). The Committee noted that further data on the XBB.1.5 vaccine in adults and adolescents would be available in early 2024.

Suitability

11.36. The Committee noted that the Nuvaxovid XBB.1.5 vaccine is intended to be supplied in a multi-dose vial that doesn't require dilution and has a nine-month shelf life. The Committee noted that once opened the vial is stable for 12 hours at 2 to 25°C. The Committee considered that using multi-dose vials increase the potential wastage of vaccine compared to single dose presentations.

Pfizer: **tozinameran, riltozinameran, famtozinameran, raxtozinameran (BNT162b2) vaccine (Comirnaty®) for the prevention of COVID-19**

Health benefit

11.37. The Committee noted that since February 2021 the tozinameran, riltozinameran, famtozinameran, raxtozinameran (BNT162b2) vaccine (Comirnaty) has been the main COVID-19 vaccine used in New Zealand. The Committee noted that the bivalent Original/ Omicron BA.4/5 vaccine was available from March 2023 and XBB.1.5 vaccine from March 2024.

11.38. The Committee considered that the randomised control trials of Comirnaty reported high vaccine efficacy against symptomatic disease, hospitalisation and death in adults (16 years and over) (Polack et al. N Engl J Med 2020;383:2603-15 and Thomas, et al. N Engl J Med 2021;385:1761-73). The Committee considered that the studies were limited by low numbers of infections in both arms and lack of inclusion of people aged 80 years and older, who are at the highest risk of death from COVID-19. The Committee noted that while the efficacy of Comirnaty persisted for at least six months, the trials were conducted in the pre-Omicron era.

11.39. The Committee noted a randomised control trial assessing the efficacy and safety of Comirnaty in adolescents that reported 100% vaccine efficacy and non-inferiority for immunogenicity, measured as geometric mean titres (GMT) ratios, when comparing 12 to 15 year olds with 16 to 25 year olds. The Committee noted that the rates of adverse events in the vaccinated and placebo groups were 3% and 2% respectively but 20% of participants experienced fever after the second dose (Frenck et al. N Engl J Med 2021;385:239-50). The Committee noted that the median follow up was two months. The Committee noted that this was a small trial and that there were no severe COVID-19 cases.

11.40. The Committee noted an unpublished randomised control trial assessing the efficacy and safety of primary vaccination course in children aged 5 to 11 years that reported vaccine efficacy of 95.0% against symptomatic infection. The Committee noted that there was 99.2% seroresponse and a 1.04 GMT ratio compared to 16- to 25-year-olds. The Committee noted that the most common adverse event was injection site pain (74% in the vaccinated group). The Committee noted that median follow up was 2.3 months.

11.41. The Committee noted a randomised control trial assessing the efficacy and safety of Comirnaty boosters in people 16 years old and over. The Committee noted that the vaccine efficacy against infection was reported to be 95.6% (95% CI, 89.3 to 98.6). The Committee noted that the rate of adverse events in the vaccine group was 25% compared to 23.4% in the placebo group. The Committee noted that the median follow up was 2.5 months (Moreira et al. N Engl J Med 2022;386:1910-21).

11.42. The Committee considered that the follow up durations across published trials of Comirnaty in adolescent and children (6 years and over) were short but expected longer-term data to become available. The Committee noted that the data for infants

and children 6 months to 5 years is not yet published (NCT04816643). The Committee noted that the phase I trial was a dose finding study and phases II and III were safety and immunogenicity trials as reported in the Medsafe datasheet (Comirnaty (maroon cap) Medsafe datasheet. Updated 15 November 2023). The Committee noted that the reported adverse events for children 6 to 23 months old were irritability (>60%), decreased appetite (> 30%), tenderness at the injection site (> 20%), injection site redness and fever (> 10%). The Committee noted that the reported adverse events for children 2 to 4 years old were pain at injection site and fatigue (>40%), and injection site redness and fever (> 10%).

11.43. The Committee noted the following studies also supplied as part of the application:

- Winkour et al. N Engl J Med 2023; 388:214-27
- Brada et al. Clin Microbiol Infect. 2023;29:918-23
- Tan et al. Lancet Infect Dis. 2023;23:901-13
- Usdan et al. Clin Infect Dis. 2023:ciad718
- Branche et al. Nat Med. 2023;29:2334-46
- Thomas et al. Vaccine. 2022;40:1483-92
- Drenko et al. Transpl Infect Dis. 2023;25:e14150
- Haranaka et al. Nat Commun. 2021;12:710
- Hui et al. Lancet Reg Health West Pac. 2022;29:100586
- Yau et al. Clin J Am Soc Nephrol. 2023;19:85-97
- Munro et al. Lancet 2021; 398: 2258–76
- Murdoch et al. Infect Dis Ther. 2023;12:2241-58
- Lazarus et al. Lancet 2021; 398: 2277-87
- Dulfer et al. Lancet Reg Health Eur. 2023:29:100628
- Fitz-Patrick et al. Vaccine. 2023;41:4190-8

11.44. The Committee was informed of a study that compared observed and expected rates of adverse events post-vaccination. The Committee noted that there was no reported increase in Guillain-Barré syndrome but there was a significant increase in the risk of myocarditis and pericarditis with mRNA vaccines Spikevax and Comirnaty (Faksova et al. Vaccine. 2024;42:2200-11).

11.45. The Committee considered that, in the current setting of variant immune escape, the purpose of COVID-19 vaccination is the prevention of severe disease. The Committee considered that the vaccination confirmation bias, also called healthy vaccinee bias, likely for trials of COVID-19 vaccines. The Committee considered that the groups vaccinated in trials are less likely to have comorbidities than the populations that ultimately receive the vaccine (high risk groups) with direct impacts on vaccine efficacy. The Committee considered that healthy vaccinee bias has an impact on the interpretation of results and extrapolation to groups not included in the trials. The Committee considered that observational studies of COVID-19 vaccines may be confounded by indication and healthy vaccinee bias simultaneously.

11.46. The Committee noted that the approval of XBB.1.5 vaccines was based on antibody neutralisation data, a presumed surrogate for efficacy, and that clinical evidence to support the efficacy of these updated vaccines is not available.

11.47. The Committee was informed of correspondence that reported data from an observational cohort study in the USA on the effectiveness of XBB.1.5 vaccines and antiviral drugs against hospital admissions and death from currently circulating SARS-CoV-2 variants (Lin et al. Lancet Infect Dis. 2024: e278-e280). The Committee noted that during this study the dominant variants changed from Omicron EG.5 to HV.1 and JN.1, and the proportion of XBB.1.5 cases declined from 9% to 4%. The Committee noted that 3315 (12.2%) of recipients received an XBB.1.5 vaccine (66% Comirnaty, 32% Spikevax). The Committee noted that the adjusted hazard ratio (adjusted for age, comorbidities, previous infection or vaccination) for people who were vaccinated with an XBB.1.5 vaccine, compared with people not vaccinated with XBB1.5 for admission to hospital was 0.69 (95% CI, 0.59-0.81) and was 0.59 for death (95% CI, 0.35-0.98). The Committee considered that the short follow-up period (3.5 months), observational design and relatively small numbers of recipients of Nuvaxovid limited the applicability of the reported findings to the New Zealand context.

11.48. The Committee were informed of an interim effectiveness analysis of XBB.1.5 vaccines in the Morbidity and Mortality Weekly Report September 2023-January 2024. The Committee noted that the report contained interim data on the effectiveness of XBB.1.5 vaccines, compared with people who did not receive an updated vaccine dose, correlating against emergency department and urgent care encounters and hospitalisations among immunocompetent adults (Link-Gelles et al. MMWR. 2024;73:271-6). The Committee noted that for ED/UC encounters vaccine effectiveness was 51% (95% CI, 47%-54%) during the first 7-59 days and 39% (95% CI, 33%-45%) during days 60-119. The Committee noted that vaccine effectiveness for people aged 65 years and over was 49% (95% CI, 44%–54%) in the first 7–59 days and 37% (95% CI, 29%–44%) in the 60–119 days after an updated dose. The Committee noted that vaccine effectiveness for hospitalisation varied from 43% to 53%, reducing to 50% for longer follow up. The Committee considered that there was relatively poor protection against infection resulting in ED visits. The Committee considered that the protection against hospitalisation was around 50% without change upon longer follow up. The Committee considered that the report was limited by not including immunocompromised people, short follow up and its non-experimental observational design.

11.49. The Committee was informed of an observational unpublished study reported vaccine effectiveness for the Comirnaty XBB.1.5 vaccine of 70% against COVID-19 hospitalisation in people over 75 years old and 73% vaccine efficacy against ICU admission in people 60 years old (van Werkhoven et al. [Preprint]. 2023).

Suitability

11.50. The Committee noted that there are approved formulations for different age groups in New Zealand: adult XBB.1.5 (12 years and over), child wild type (5-11 years) and infant wild type (6 months to 4 years). The Committee noted that the XBB.1.5 variant formulation was currently limited to people aged 12 years and over regardless of previous vaccination status. The Committee considered that the multidose vials would create more wastage than single use vials, but single dose vials or prefilled syringes would use more storage space.

11.51. The Committee noted that the XBB.1.5 variant vaccines do not require dilution. The Committee noted that unopened vials can be store for up to 18 months at -90°C to -60°C stored at 2°C to 8°C for up to 10 weeks once thawed. The Committee noted that opened or unopened vials can be stored at room temperature (8ºC to 30ºC) for up to 12 hours.

Costs and Savings

11.52. The Committee considered a cost utility analysis included as part of the application. The Committee noted that the analysis did not vary the vaccine efficacy between ages and comorbidities. The Committee considered that there is a difference in vaccine efficacy between ages and comorbidities and it appropriate to reflect this in future economic modelling of COVID-19 vaccines.

11.53. The Committee considered that future economic modelling of COVID-19 vaccines should use hospitalisation and case data from the last year, as data from earlier periods would not be reflective of the level of hybrid immunity in the New Zealand population against the background of current prevalent circulating variants.

CSL-Seqirus: **ARCT-154 for the prevention of COVID-19**

Health benefit

11.54. The Committee noted that ARCT-154 is composed of self-amplifying mRNA encapsulated in a nanoparticle. The Committee noted that the mRNA encodes a replicase and the prefusion-stabilised, furin-cleavage-site-inactivated, spike glycoprotein of the G clade D614G variant of SARS-CoV-2. The Committee noted that the spike glycoprotein is expressed within transfected cells, resulting in B and T cell responses, including neutralising antibodies. The Committee considered that although the mechanism of action differs in some ways from Comirnaty, it is unknown if those who cannot have Comirnaty can have ARCT-154. The Committee considered that this formulation is unlikely to appeal to people who do not want to have existing RNA vaccines.

11.55. The Committee noted that the vaccine is delivered as an intramuscular injection as a primary series (two doses 4 weeks apart) and as a booster (one dose at least 3 months after last prior dose of a COVID-19 vaccine).

11.56. The Committee noted that this vaccine is approved in Japan for people over 18 years. The Committee noted that at the time of the meeting the European Medicines Authority (EMA) was evaluating the vaccine. The Committee noted that the vaccine is not currently registered with Medsafe for any indications. The Committee noted that the supplier indicated that a Medsafe registration would be lodged imminently.

11.57. The Committee noted an unpublished phase I, II and III, randomised, double-blind trial in volunteers 18 years or older assessing vaccine efficacy against symptomatic, and severe disease in Vietnam (Hồ et al. Preprint. Peer-reviewed version not published). The Committee noted that the trial included participants at greater risk of severe COVID-19 due to comorbidities (34.9%) and people aged 60 years and older (17.4%). The Committee noted that the vaccine efficacy against any confirmed COVID-19 (Days 36-92 post vaccination) of 56.6% (95% CI, 48.7 to 63.3) and vaccine efficacy against severe disease of 95.3% (95% CI, 80.5 to 98.9) and death of 86.5% (95% CI, -7.4 to 98.3). The Committee considered that the vaccine was moderately effective at preventing COVID-19 (between Days 36-92 post vaccination) and was highly effective at preventing severe disease. The Committee noted that local and systemic adverse reactions were common with ARCT-154 and there were no vaccine-related severe adverse events. The Committee considered that this study was conducted when the Delta variant was widely circulating.

11.58. The Committee noted a trial assessing the immunogenicity of a fourth dose (booster) of ARCT-154 compared to Comirnaty (Oda et al.Lancet Infect Dis. 2023:S1473-3099(23)00650-3). The Committee noted that the participants of this trial were aged 18 years or over and previously immunised with three doses of either Comirnaty or mRNA-1273, with the last dose being Comirnaty and received at least 3 months prior to trial inclusion. The Committee noted that ARCT-154 was reported to be non-inferior

to a fourth dose of Comirnaty against the wild-type variant (original Wuhan) when comparing neutralising antibody geometric mean titres (GMT) (ratio at day 28 days after boosting: 1.43 (95% CI, 1.26-1.63)) and seroresponse (difference at day 28 days after boosting: 13.6% (95% CI 6.8-20.5)). The Committee noted that the ARCT-154 was reported to be non-inferior to Comirnaty against Omicron BA.4/5 variants when comparing neutralising antibody geometric mean titres (GMT) (ratio at day 28 days after boosting: 1.3 (95% CI, 1.07-1.58)) and seroresponse (difference at day 29: 11.6% (95% CI 4.9-18.3)). The Committee noted that local and systemic events were similar in severity and frequency to Comirnaty, with no reports of solicited local reactions or of systemic adverse events described as grade 4 or life-threatening. The Committee noted that there was one report of abnormal hepatic function in the ARCT-154 group related to the vaccine. The Committee noted one report of chest pain in the ARCT-154 group and three in the Comirnaty group.

11.59. The Committee noted that an ongoing trial assessing the persistence of the immune response of ARCT-154 compared to Comirnaty after a fourth dose (booster) at three and six months post-fourth dose (Oda et al. Lancet Infect Dis:S1473-3099(24)00060-4). The Committee noted that at day 181, GMT ratio against the wild type variant for ARCT-154 compared to Comirnaty was 2.21 (95% CI, 1.91-2.57) and against BA.4/5 variant was 2.26 (95% CI, 1.78-2.86). The Committee considered that ARCT-154 likely had better persistence of neutralising antibodies out to 12 months (although this data is not yet available).

11.60. The Committee noted that there was much less evidence to support the consideration of this vaccine and that its use was limited to the Japanese market. The Committee considered that in order to fully assess this vaccine for funding, further data would be required regarding:

11.60.1. immunogenicity and efficacy of the vaccine against currently circulating variants

11.60.2. duration of protection, particularly against severe disease

11.60.3. post-marketing data on safety, immunogenicity, and efficacy.

Suitability

11.61. The Committee noted that each dose is 0.5 mL in volume and contains 5 mcg of mRNA that is administered via intramuscular injection. The Committee noted that the vial is a single dose vial that requires reconstitution with saline. The Committee noted that vials must be stored in a freezer between -15°C to -25°C.

11.62. The Committee noted that there was no information provided on the shelf-life upon reconstitution, at room temperature or in the fridge (-2°C to -8°C), whether vials can be refrozen or how they are required to be handled during transportation.

COVID-19 vaccine procurement

Funding of COVID-19 vaccines

11.63. The Committee considered that all the COVID-19 vaccines and technology platforms considered at this meeting would be suitable to be included in a procurement process for COVID-19 vaccines.

11.64. The Committee considered that it would like to see more mature safety and efficacy data for self-amplifying mRNA vaccines,

11.65. The Committee considered it to be reasonable to have a single funded vaccine platform available for eligible people in Aotearoa New Zealand. The Committee considered it desirable to have access to a second funded vaccine platform for

people who cannot have or have experienced intolerable adverse reactions to the other funded vaccine technology.

11.66. Under a Dual Supply arrangement two or more suppliers would be awarded contracts to supply funded COVID-19 vaccines to New Zealand, and clinicians and patients would be able to choose which funded vaccine to use.

11.67. The Committee considered that either a PSS or a Dual Supply arrangement would be an acceptable outcome from a competitive procurement process for COVID-19 vaccines.

11.67.1. The Committee considered that people who have hypersensitivity to any of the components of a vaccine would be contraindicated for that particular vaccine. People who have experienced adverse events or have other intolerable side effects would not be recommended to have that particular vaccine.

11.67.2. The Committee considered at this stage that people who have experienced myocarditis, pericarditis or experienced other intolerable adverse events should not be revaccinated with an mRNA vaccine.

11.67.3. The Committee noted the early development stage of self-amplifying mRNA vaccines. It considered that there was not yet sufficient safety data accumulated to identify any groups who could not receive a self-amplifying mRNA vaccine.

11.67.4. .

11.67.5. .

11.67.6. The Committee considered that if only one vaccine technology was funded, many people who could not tolerate the funded vaccine would still have the option of anti-viral therapy if they developed COVID-19 (ie. they would meet the eligibility criteria for funded community COVID-19 antivirals). The Committee considered that the risks of not being vaccinated may change over time as the SARS-CoV-2 virus evolves, including immune escape and any changes in virulence.

11.68. The Committee considered the benefits and risks associated with having different vaccines or technology platforms for different eligible populations to be unclear. The Committee considered that more complex vaccine schedules would create greater risk of administration errors. The Committee considered the following to be important when evaluating vaccines in any commercial process:

11.68.1. immunogenicity and efficacy of the vaccines, including against currently circulating variants.

11.68.2. availability of post-marketing data on safety, immunogenicity, and efficacy.

11.68.3. duration of protection.

11.68.4. protection against developing long-COVID and the associated morbidity.

11.69. The Committee noted that combination vaccines of COVID-19, influenza and/or respiratory syncytial virus components were in development. The Committee recommended it review these combination vaccines if suppliers submit funding applications to Pharmac.

11.70. The Committee noted that there are currently no COVID-19 vaccines available for purchase privately by individuals who are not eligible for funded vaccination. The Committee considered it would be advantageous for people not eligible for funded vaccines to have the option to purchase vaccine if they wished. The Committee noted

that it is suppliers who will decide whether they will support a private market for vaccines. The Committee considered the uptake of privately purchased vaccine would likely be driven by the retail price and that there would be affordability-related inequity in access to the vaccine.

Evidence for COVID-19 vaccine efficacy

11.71. The Committee noted vaccine protection from symptomatic SARS-CoV-2 infection is strongly correlated with neutralising antibody (nAb) titres (noting Gilbert et al. Science. 2022;375:43-50, Feng et al. Nat Med. 2021;27:2032-40; Fong et al. Nat Microbiol. 2022;7:1996-2010; Bergwerk et al. N Engl J Med. 2021;385:1474-1484) and that high nAb titres have been accepted by a number of national immunisation technical advisory groups and regulatory bodies (including the Australian Technical Advisory Group on Immunisation [ATAGI] and Medsafe) as a correlate of protection. However, this evidence informing correlates of protection was largely confined to protection against ancestral variants of SARS-CoV-2.

11.71.1. The Committee noted that, for context, XBB.1.5 vaccines were approved based only on immune surrogate nAb data, without confirmatory clinical evidence of vaccine efficacy at the time.

11.71.2. The Committee noted that a similar approach is taken with the annual seasonal strain updates for influenza vaccines setting, where new variants were included in annual vaccine updates. The Committee noted that international consensus is that a similar approach will occur with future COVID vaccines.

11.72. The Committee noted immunogenicity bridging studies measuring nAb titres have been used to infer equivalent effectiveness of new variant vaccines.

11.73. The Committee considered there to be insufficient evidence currently to define a protective nAb titre threshold against SARS-CoV-2 infection or severe disease, as studies that had reported significant relationships between neutralisation titres and vaccine efficacy had used different methods, data from different clinical trials, and neutralisation data derived from different assays (noting eg. Khoury et al. Nat Med. 2021;27:1205-11; Gilbert et al. 2022, Feng et al. 2021; Bergwerk et al. 2021).

11.74. The Committee considered that while it was possible to infer the vaccine effectiveness of COVID-19 vaccines against current and future variants based on nAb titres induced by those vaccines, a major limitation of these calculations would be their reliance on antibody results based on ancestral variants on SARS-CoV-2 and the considerable heterogeneity between studies informing those correlates. The Committee considered this to be a source of material uncertainty for future assessments of COVID-19 vaccines.

11.75. The Committee considered that it was not possible directly compare antibody geometric mean titres (GMTs) across studies of vaccine technology platforms to infer whether any one platform elicits greater protection from infection or severe disease, due to the variation between study designs, assays, measurement techniques.

11.76. The Committee noted that while nAb titres were an important measure of adaptive immunity, it was unknown how aspects of cell-mediated immunity may differ between the different technology platforms.

Suitability considerations for COVID-19 vaccines

11.77. The Committee noted vaccines can be packaged as multi-dose vials, single dose vials or single dose prepared syringe-needle systems.

11.78. The Committee considered multi-dose vials to be advantageous if used in large clinics and take up less storage space compared to single dose vials and pre-filled

syringes. The Committee considered that there would, however, be considerable wastage in rural areas if multi-dose vials were the only option available.

11.79. The Committee considered the pre-filled syringes to take up the most room in storage but are also the most convenient option for administration. They do not require re-constitution by the healthcare provider.

11.80. The Committee noted the long-term storage facilities are different for each of the vaccine platforms. Long term storage needs of current vaccines are for ultra-low temperature freezer or refrigeration (2 to 8°C).

11.81. The Committee considered ultra-low temperature freezer storage may be limited in different areas of New Zealand and vaccines that require the usual 2 to 8°C cold chain refrigerator temperature conditions would be more feasible for vaccine administration.

11.82. The Committee considered wastage due to expiry can be significant and that vaccines with longer ‘in-use’ or ‘ready-to-be-administered’ shelf-lives would be advantageous.

11.83. The Committee considered there to be risks of incorrect dosing if there is more than one vaccine available, but considered this would need to be balanced with the risk in having only one vaccine to supply the market if there is a supply shortage.

11.84. The Committee noted that it is suppliers who are ultimately responsible for updating Medsafe datasheets. The Committee considered it important that COVID-19 vaccine datasheets be kept updated with emerging evidence and advice, and encouraged suppliers work with Medsafe on this. The Committee considered that the impact on cold-chain storage would need to be considered if a different COVID-19 vaccine was funded in New Zealand.

11.85. The Committee considered that if a different COVID-19 vaccine was funded in New Zealand, adequate lead time would be required to ensure healthcare providers had sufficient access to resources and training.