# 5 Coronavirus disease (COVID-19)

## Key information

<table>
<thead>
<tr>
<th>Mode of transmission</th>
<th>Aerosolised droplets.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incubation period</td>
<td>Most commonly 2–5 days (range 1–14 days).</td>
</tr>
<tr>
<td>Period of communicability</td>
<td>From 1–2 days before, and typically transmissibility peaks 5 days after symptom onset. Asymptomatic spread is documented.</td>
</tr>
<tr>
<td>Incidence and burden of disease</td>
<td>Global pandemic ongoing. The burden of disease predominantly lies with older adults, those with comorbidities and health care workers exposed to patients with high viral loads. Children generally experience milder disease</td>
</tr>
</tbody>
</table>
| Dose, presentation, route | mRNA CV: Comirnaty  
• 0.3 mL dose  
• multi-dose vial, to be diluted before use  
• intramuscular injection  
• Storage once thawed:  
  - undiluted, +2°C to 8°C expiry 1 month (31 days)  
  - diluted, +2°C to 30°C expiry 6 hours.  
ChAd-CV: COVID-19 Vaccine AstraZeneca  
• 0.5 mL dose  
• Multi-dose vial, no dilution required  
• Intramuscular injection  
• Storage: +2°C to 8°C (up to 6 months)  
  - Expiry after 48 hours once cap has been removed at +2°C to 8°C  
  - Use drawn up vaccine within 5 hours (and before expiry) |
| Funded vaccine indications and schedule | Two doses of mRNA-CV, given at least 21 days apart:  
• for use from age 12 years  
• a third primary dose given at least 8 weeks after first two doses for those with severe immunocompromise  
• a booster dose given at least 6 months after completion of primary course from age 18 years for all |
| Other funded vaccine indication and schedule | Two doses of ChAd-CV, given from 4 to 12 weeks apart for use from age 18 years |
## Contraindications

mRNA-CV and ChAd-CV: A history of anaphylaxis to any component or previous dose.

ChAd-CV: A history of capillary leak syndrome, thrombosis with thrombocytopenia to previous dose.

## Precautions

mRNA-CV and ChAd-CV: A definite history of anaphylaxis to any other product is a precaution not contraindication.

mRNA: Defer further doses if individual develops myocarditis/pericarditis after first or second dose of mRNA-CV.

ChAd-CV is not recommended for use during pregnancy. A history of thrombosis, certain prothrombotic autoimmune diseases, thrombocytopenia is a precaution.

## Potential responses to vaccine

mRNA and ChAd-CV: Generally mild or moderate: injection site pain, headache, fever, muscle aches, dizziness and nausea, a day or two after vaccination. For mRNA-CV, these responses are more commonly reported after second dose and in younger adults (<55 years). For ChAd-CV, responses are more commonly reported after first dose.

## Vaccine effectiveness

mRNA-CV: Data from a phase III clinical trial showed efficacy against confirmed symptomatic COVID-19 to be 90–98% after two doses. Real-world data showed similar effectiveness. Effectiveness is maintained against severe disease caused by SARS-CoV-2 variants, including Delta.

ChAd-CV: Pooled data from four phase III clinical trials gave overall efficacy against symptomatic COVID-19 of 41-75.7% after doses. Effectiveness of 61-72% against symptomatic disease and of 75-97% against hospitalisation with Delta variant.

Effectiveness of both vaccines shows waning, particularly against mild disease and for elderly, from several months after the primary course.

## Public health measures

Ongoing rapid contact tracing and testing for all suspected cases and their close contacts. Quarantine and isolation of close contacts and cases. Control measures differ according to vaccination status.

### 5.1 Virology

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a member of the Coronaviridae family and the Betacoronavirus genus. This enveloped, positive-strand RNA virus encodes four major structural proteins – spike (S), membrane (M), envelope (E) and a helical nucleocapsid (N). To enter host cells, the spike protein, which forms the characteristic crown-like (Latin: corona) surface structures, binds to the angiotensin-converting enzyme-2 (ACE2) receptor most frequently found on human respiratory tract epithelium.¹ ²

The precise origin of this virus is unknown. First identified in humans in Wuhan, China, this virus shares a strong genetic sequence similarity to bat coronaviruses found in China,³ and is a suspected zoonosis from bats via an intermediary animal, such as a pangolin.⁴ As with most RNA viruses, mutations occur and variant strains of SARS-CoV-2 have been identified.
5.2 Clinical features

Coronavirus disease 2019 (COVID-19) is caused by the SARS-CoV-2 virus, which infects the respiratory tract and is transmitted human to human primarily through respiratory droplets and aerosols. Documented transmission has also occurred through direct contact and rarely fomites (objects or materials that can carry infection).

The reproduction number ($R_0$) (see section 1.2.1) was initially estimated to be around 2–3.\(^5\)\(^6\) Transmissibility varies by setting, and recently identified variant strains of SARS-CoV-2 have been well beyond the initial estimated $R_0$ values.\(^7\)\(^8\) The globally dominant Delta (B1.617.2) variant is twice as transmissible as the ancestral strain ($R_0$ 5–6).\(^9\)

The symptoms of COVID-19 range widely from asymptomatic or a mild respiratory tract infection to severe and pneumonia, which can lead to severe inflammatory disease and respiratory failure. The most common symptoms of COVID-19 are like those of other common respiratory illnesses and include a new or worsening dry cough, sneezing and rhinorrhoea or nasal congestion, fever, sore throat and shortness of breath. Unlike other respiratory viral infections, COVID-19 is frequently associated with a temporary loss of smell or altered sense of taste, and sometimes this is the only symptom. Some cases have reported gastrointestinal symptoms including nausea, diarrhoea, vomiting and abdominal pain, headache, muscle aches, malaise, chest pain, joint pain, and confusion or irritability; these symptoms almost always occur with one or more of the common symptoms. For around 80 percent of cases, COVID-19 is a mild disease, but some develop more severe disease, particularly older adults, pregnant people and those with comorbidities, which can progress to multi-organ and respiratory failure. As for influenza and other respiratory viruses, many of those with laboratory-confirmed infection remain asymptomatic.

In the early stages, it is difficult to distinguish COVID-19 from other common viral infections and, as of early 2021, the most reliable diagnostic test has been detection of viral mRNA from a nasopharyngeal swab, using PCR assay. Further methods of testing (such as saliva sampling and rapid antigen/lateral flow tests) are being increasingly used. SARS-CoV-2 serology can help distinguish historic disease from mild current symptoms but is not in routine use.

The incubation period is typically around two to five days (up to 14 days). Individuals may be infectious from up to two days before becoming symptomatic, with infectiousness typically peaking within five days of symptom onset.\(^10\) High viral loads are detected in the nose at time of symptom onset.\(^11\) Viable virus is not usually detectable for more than ten days after symptom onset, although SARS-CoV-2 mRNA has been detected for up to 83 days in respiratory and stool samples.\(^10\)\(^12\) Unlike previous coronavirus outbreaks (SARS and MERS), transmission of SARS-CoV-2 can also occur before the onset of symptoms or from asymptomatic individuals.\(^13\) Viral loads and infectiousness are highest immediately after symptom onset, and most transmission occurs in household settings.\(^14\)\(^15\)

It is currently unclear what protection previous infection with SARS-CoV-2 provides. A study in the UK in health care workers found protection against symptomatic COVID-19 to be similar to that reported for mRNA COVID-19 vaccine.\(^16\) A previous history of SARS-CoV-2 infection was associated with an 83 percent lower risk of infection, with a
median time to re-infection of over five months. Only about one third of the reinfections in health care workers presented as typical COVID-19 symptoms, as compared with 78 percent of new infections. Neutralising antibodies have been detected and remained relatively stable between eight to 11 months after primary infection, even without natural boosting as in New Zealand.

5.2.1 Children and young adults

The evidence around disease in children and adolescents is more limited. Data suggests most younger people, particularly children under 10 years old, have asymptomatic or mildly symptomatic infections with a small proportion at high risk of severe disease. As more adults are vaccinated and with more widespread disease spread, severe outcomes in children are emerging. In the US as of 18 November, 25 percent of COVID-19 cases were in children, 1.7–4.0 percent of cases hospitalised were children, and is increasing. The role children play in transmitting SARS-CoV-2 is still unclear and is changing as new variants evolve and older populations are increasingly vaccinated.

5.2.2 Risk groups

Risk factors for severe disease include older age, male, smoking, obesity and chronic medical conditions, including type 2 diabetes mellitus, cancer, chronic respiratory disease, cardiovascular disease, chronic kidney disease, hypertension and being immunocompromised. Increased incidence is well documented in some ethnic groups but seems primarily related to prevalence of the risk factors listed above. Increasing age is the most important risk factor for severe disease, due to declining immune function and high prevalence of comorbidities. The highest rates of mortality are in the oldest age groups, especially those aged over 80 years (at a rate 20-fold higher than for those aged 50–59 years in the United Kingdom).

Health care workers

Patient-facing health care workers caring for patients with COVID-19 are likely to be exposed to higher viral loads, placing them and their household members at greater risk of developing COVID-19 than the general population. In Scotland, one-sixth of the COVID-19 cases admitted to hospital were health care workers and their household members. Health care workers have also been implicated in the spread of SARS-CoV-2 within health and long-term care facilities. However, the use of personal protective equipment (PPE) and other measures aimed at reducing nosocomial viral transmission have been shown to be effective, such that, where COVID-19 is prevalent in the community, health care workers are more likely to catch COVID-19 from an infected household member.
Pregnant women

Although pregnant women are not at increased risk of SARS-CoV-2 infection, they are at increased risk of severe disease and death compared with age-matched non-pregnant women.\textsuperscript{27, 28} While the absolute risk of severe outcomes among pregnant women is low compared with absolute risk due to advanced age, the rate of ICU care for COVID-19 has been found to be three-fold higher (adjusted risk ratio 3.0; 95\% CI 2.6-3.4) for pregnant women than for non-pregnant women,\textsuperscript{29} and the case-fatality rate in one United States study was 13.6-fold higher for pregnant women.\textsuperscript{28} Obesity, hypertension, asthma, autoimmune disease, diabetes and older age are also associated with severe COVID-19 in pregnant women.\textsuperscript{30}

Infants of mothers with COVID-19 are at increased risk of preterm birth and neonatal ICU admission.\textsuperscript{30} Early studies do not suggest intrauterine transmission, but transmission during birth has been shown in around 3 percent of neonates.\textsuperscript{31} Most neonatal infections are asymptomatic or mild, but around 12 percent experience severe disease with dyspnoea and fever as the most commonly reported signs.\textsuperscript{32}

5.2.3 Post-infection complications

Longer lasting effects of infection have been reported, described as ‘long-COVID’. Long-COVID appears to affect around 10 percent of those infected, particularly those with at least five symptoms in the first week of illness.\textsuperscript{33, 34, 35} Post-acute manifestations include cardiovascular, pulmonary and neurological effects, including chronic fatigue, dyspnoea, specific organ dysfunction and depression.\textsuperscript{36} Paediatric multisystem inflammatory syndrome (PIMS-TS or MIS-C) has been temporally and rarely associated with largely asymptomatic SARS-CoV-2 infection in children and adolescents.\textsuperscript{37, 38}

5.2.4 SARS-CoV-2 variants

As with all viruses, new variants have evolved. Most recently, certain variants have been shown to bind the ACE2 receptor more readily, making the variants more transmissible. It is unclear whether these variants result in more cases of severe disease, but irrespectively, the greater numbers of people becoming infected is increasing the burden of the disease.\textsuperscript{7, 8} There is evidence that recent variants (eg, Delta) are more transmissible than the former strains.\textsuperscript{9, 39} The CDC has classified genetic variants in to three classes:\textsuperscript{40}

- Variants of interest – specific genetic markers that are predicted to affect transmission, diagnostics, therapeutics or immune escape (for example, reduced antibody neutralisation).
- Variants of concern – evidence of increased transmissibility, more severe disease, reduction in antibody neutralisation, reduced vaccine or treatment efficacy or diagnostic detection failures.
- Variants of high consequence – clear evidence that prevention measures or medical countermeasures have significantly reduced effectiveness.
5.3 Epidemiology

5.3.1 Global burden of disease

Clusters of distinctive pneumonia cases were observed in Wuhan, China during December 2019. The cause was identified in January 2020 as a novel coronavirus that had genetic and clinical similarity to the coronavirus causing the severe acute respiratory syndrome (SARS) epidemic from 2002 to 2004. Consequently, the novel coronavirus was named SARS-CoV-2 and the associated disease named Coronavirus Disease 2019 (COVID-19). Due to the rapid spread, a public health emergency of international concern (PHEIC) was announced in late January 2020. By the time the COVID-19 pandemic was declared by the World Health Organization (WHO) on 11 March 2020, there were 118,000 reported COVID-19 cases and 4,291 associated deaths in 114 countries. The global death toll surpassed one million by late September 2020.

As of 21 November 2021, over five million deaths and around 255 million confirmed cases were reported to the WHO, around three million new cases per week continue to be reported. The Americas, Europe and South-East Asia have the highest numbers of recorded cases (96 million in the Americas and 84 million in Europe, South-East Asia 44 million cases) and ten million cases were reported in the Western Pacific region. See the WHO Coronavirus Disease (COVID-19) Dashboard (covid19.who.int) for the latest official data. Actual rates are expected to be considerably higher than officially reported rates.

The infection-fatality rate, while still high particularly in the older age groups, has reduced since the start of the pandemic, with improved clinical recognition and management and the use of therapies of demonstrated value, such as dexamethasone (see Figure 5.1).^{41,42}
The use of vaccines is anticipated to reduce the global burden of COVID-19 significantly. The first phase I clinical trial for a COVID-19 vaccine commenced in March 2020. The first public vaccination dose was given as part of a mass campaign in the United Kingdom on 8 December 2020. As of 21 November 2021, over 7.4 billion doses had been administered with 3.1 billion people fully vaccinated.

See the WHO Coronavirus Disease (COVID-19) Dashboard (covid19.who.int) and the Our World in Data website (ourworldindata.org/covid-vaccinations) for the latest official data.

5.3.2 New Zealand epidemiology

According to ESR data, as of 30 November 2021, 11,075 confirmed cases and 30 deaths associated with COVID19 have been notified in New Zealand since 24 February 2020. Most cases were observed in those aged 20–34 years (3,464 cases, 33%), 35–49 years (2,108, 20%) and 50–64 years (1,414, 13 percent). Children aged 5–19 years represent a higher proportion (22 percent) those infected during the most recent outbreak, from 17 August 2021, than previously seen which is likely due to household transmission of the Delta variant. In total, there have been 2,132 cases (21 percent) in children aged 5–19 years, 561 cases (6 percent) aged 1–4 years and 141 cases (1.4 percent) aged under 1 year. To date (29 November 2021), 27 children (2 percent of cases aged under 12 years have been admitted to hospital for COVID-19 in New Zealand. Cases during this outbreak have been predominantly Māori (45 percent), with Pacific Peoples (29 percent), European or Other (18 percent) and Asian (6 percent).
Prior to the outbreak of the Delta variant, during 2021, most of the reported cases were imported from overseas (over 95 percent from 1 January to 9 August 2021) as shown in Figure 5.2. During the Delta outbreak (from 17 August) the majority of cases were locally acquired and epidemiologically linked, and a lower proportion were imported (4 percent). According to the Ministry of Health, a total of nearly 4.9 million tests were conducted from 22 January 2020 (the date of the first test in New Zealand) to 29 November 2021. Of these, 12,160 tests (0.3 percent) in the community and 1,777 tests (0.4 percent) in managed facilities were positive for SARS-CoV-2.

**Figure 5.2: Pooled weekly confirmed COVID-19 cases by source, 24 February 2020 to 21 November 2021**

![Graph showing pooled weekly confirmed COVID-19 cases by source, 24 February 2020 to 21 November 2021](image)

Source: ESR


**Strategy for prevention**

The first case of COVID-19 was reported in New Zealand on 28 February 2020. During March, cases numbers increased, and clusters of transmission were identified. Border restrictions were implemented on 16 March 2020. On 25 March 2020, New Zealand entered a nationwide lockdown (alert level four).

New Zealand implemented an elimination strategy with four defined levels of pandemic response to prevent the spread of SAR-CoV-2. A mobile phone app aided rapid contact tracing. For further information about the country’s alert system levels, see covid19.govt.nz/alert-system/about-the-alert-system.
These strategies were effective in containing the spread of SARS-CoV-2 in New Zealand (see case curve for 24 February to 8 June 2020 at nzcoviddashboard.esr.cri.nz for details). These restrictions were able to rapidly stop the spread of the virus within the country. Only 19 percent of the introductions of virus in 2020 resulted in ongoing transmission or more than one additional case.5

5.4 Vaccines

5.4.1 Introduction

Clinical trials for COVID-19 vaccine candidates began shortly after the pandemic was announced in March 2020. Between October to December 2020, the New Zealand Government signed advanced purchase agreements for four vaccine candidates, with purchase dependent on approval for use from the New Zealand Medicines and Medical Devices Safety Authority (Medsafe). This is an ongoing process and, therefore, the availability and eligibility for these different vaccines may change. Provisional consent allows for changes to age groups and use, such as booster doses, which is not possible once Full consent is granted.

5.4.2 Available vaccines

Vaccines for COVID-19 continue to undergo phase III clinical trials, and the Medsafe review process is ongoing for each vaccine candidate. Provisional consent approval was granted for use of New Zealand’s first COVID-19 vaccine on 3 February 2021, namely, a mRNA-based COVID-19 vaccine (mRNA-CV, trade name Comirnaty) manufactured by Pfizer/BioNTech. In addition, two adenoviral vector COVID-19 vaccines were also granted provisional approval in July 2021: COVID-19 Vaccine AstraZeneca (available from late November 2021) and COVID-19 Vaccine Janssen (not yet available in New Zealand).

Funded vaccines

The mRNA-CV consists of messenger ribonucleic acid (mRNA) encoding the full-length spike glycoprotein of the SARS-CoV-2 virus inside a lipid nanoparticle. The spike protein has an adjuvant effect, so no additional adjuvant is included. It is designated BNT162b2 in clinical trials conducted by Pfizer and BioNTech. This mRNA vaccine delivers the instructions for human cells to build the viral antigen, SARS-CoV-2 spike protein. The mRNA is temporarily protected from degradation by the lipid nanoparticle that also facilitates fusion with the recipient’s cell wall.43,44

An adenoviral vector COVID-19 vaccine (COVID-19 vaccine AstraZeneca; also known as Vaxzevria) was provisionally approved for use in New Zealand on 29 July 2021. It is manufactured by AstraZeneca (clinical trial designation AZD122). This vaccine (abbreviated here to ChAd-CV) contains a recombinant non-replicating chimpanzee adenovirus, ChAdOx1-S, contain a transgene encoding the prefusion SARS-CoV-2 spike
glycoprotein. The adenovirus delivers the instructions to make replicas of the SARS-CoV-2 viral protein – it has been modified to be unable to replicate and only the gene encoding the spike protein (the antigen) can be expressed. Once the protein instructions have been delivered virus is destroyed.

mRNA-CV (Comirnaty, Pfizer/BioNtech)

Each 0.3 mL dose of mRNA-CV contains:
- 30 µg of single-stranded 5'-capped mRNA encoding pre-fusion stabilised SARS-CoV-2 full-length spike glycoprotein embedded in a lipid nanoparticle. The mRNA is produced using cell-free in vitro transcription from DNA templates.
- The lipid nanoparticle contains ALC-0315 \(((4\text{-hydroxybutyl})\text{azanediyl})\text{bis(hexane-6,1-diyl)}\text{bis(2-hexyldecanoate)}\), ALC-0159 \((2\text{-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide)}\), distearoylphosphatidylcholine (DSPC)) and cholesterol.
- Also contains potassium chloride, monobasic potassium phosphate, sodium chloride, dibasic sodium phosphate dihydrate, sucrose and water for injection.

ChAd-CV (COVID-19 Vaccine AstraZeneca or Vaxzevria)

Each 0.5 mL dose of ChAd-CV contains:
- $5 \times 10^{10}$ viral particles of ChAdOx1-S (recombinant, replication deficient chimpanzee adenovirus encoding the SARS-CoV-2 spike glycoprotein)
- Also contains approximately 2 mg ethanol, L-histidine, L-histidine hydrochloride monohydrate, magnesium chloride hexahydrate, polysorbate 80, sucrose, sodium chloride, disodium edetate dihydrate (EDTA) and water for injection.

Other vaccines

Another adeno-viral vector COVID-19 vaccine (Ad26.COV2.S, brand name COVID-19 Vaccine Janssen) was approved for use in New Zealand on 7 July 2021. Using a similar platform to ChAd-CV, this vaccine (abbreviated here to Ad26-CV) contains a modified non-replicating human adenovirus, Ad26, that carries a transgene coding for the COVID-19 prefusion SARS-CoV-2 spike protein. This vaccine is not currently available in New Zealand.
5.4.3 Efficacy and effectiveness

mRNA COVID-19 vaccine – Comirnaty (Pfizer/BioNTech)

Immunogenicity

Assessing immunogenicity was a key component of the early-phase clinical trials of COVID-19 vaccines before the phase III efficacy studies were conducted. Virus neutralising antibody responses measured the killing of live SARS-CoV-2 and/or pseudo-virus in cell culture. Since no correlates of protection have yet been established, humoral responses were compared with human convalescent sera collected from patients who had recovered from COVID-19.

Two vaccine candidates were evaluated (BNT162b1 and BNT162b2) in the initial phase I and II clinical trials. Both demonstrated similar dose-dependent neutralising antibody titres, which were similar or higher to the titres in convalescent sera. Anti-receptor binding domain (anti-RBD) IgG antibodies also increased with dose. As seen for other vaccines, the antibody response was lower in older people (aged 55–85 years) than in younger people (aged 18–55 years), but both groups had higher average neutralising antibody levels than those with prior SARS-CoV-2 infection.

The immunogenicity of mRNA-CV in adolescents aged 12–15 years was non-inferior to those aged 16–25 years in a phase III clinical trial. The neutralising antibody response in 190 adolescents was higher than in 170 young adults (geometric mean ratio 1.76; 95% CI 1.47–2.10).

Efficacy – clinical trial data

Efficacy of mRNA-CV (BNT162b2) was assessed in the phase III component of a large clinical trial in which 43,448 participants aged 16–85 years in Argentina, Brazil, Germany, Turkey, South Africa and the United States were randomised to receive vaccine or saline placebo. Two doses were given 21 days apart. According to interim data, vaccine efficacy (VE) against symptomatic PCR-confirmed COVID-19 was 94.8 percent (95% CI: 89.8–97.6%); eight cases in the vaccinated group and 162 cases in control group developed COVID-19 at least seven days after dose two. Evidence of previous SARS-CoV-2 infection did not alter this efficacy (VE 95.0% without and 94.6% including those with previous infection). Similar efficacy (90–100 percent) was observed across all subgroups as defined by age, sex, race, ethnicity, baseline body-mass index (35% of participants were obese, BMI ≥ 30) and the presence of at least one co-existing medical conditions (in 21%). Moderate early protection against COVID-19 was observed before the second dose. This clinical trial is ongoing, and further data is anticipated as predefined endpoints are reached. The trial is due to be completed in January 2023.

The observed vaccine efficacy for mRNA-CV in adolescents aged 12–15 years during a phase III clinical trial was 100 percent (95% CI 75.3–100) against symptomatic COVID-19. A total of 2,220 randomised participants received two doses of vaccine or saline placebo given 21 days (19–42 days apart. No cases of severe COVID-19 were observed in this age group.
Effectiveness – real-world experience

Early data from Israel at the start of its national COVID-19 immunisation programme, which included around 1.2 million vaccinated and unvaccinated individuals aged from 16 years, demonstrated that mRNA-CV was highly effective at preventing COVID-19 and severe disease, and these data were in line with those observed during clinical trials. See Table 5.1 for comparison.

In the UK, a single dose of mRNA-CV was associated with a significant reduction in symptomatic COVID-19 cases in older adults (aged from 70 years) for at least six weeks. Vaccine effectiveness was observed from 10–13 days after vaccinations, by days 28–34 vaccine effectiveness reached 70 percent (95% CI 59–78 percent), then plateauing to 61 percent (51–59 percent). Additionally, those that had been vaccinated were 43 percent (33–52 percent) less likely to require emergency hospitalisation and at 51 percent (37–62 percent) lower risk of death. A second dose (given 12 weeks after dose one) provided further protection against symptomatic disease (at day 14, vaccine effectiveness reached 89 percent (85–93 percent)).

Effectiveness against transmission

Effectiveness of mRNA-CV against transmission of SARS-CoV-2 is unclear and likely to depend on a range of factors, including rate of viral growth once infected. It is expected that fewer symptomatic people producing virus for a shorter time, the spread of the virus will decrease. Evidence from the UK has shown that vaccination against COVID-19 reduces the risk of infection with the Delta variant and accelerates the viral clearance. Although peak viral loads were similar between infected vaccinated and unvaccinated individuals, which can efficiently transmit virus within households, the secondary attack rate between household contacts was 25 percent (95% CI 18–33 percent) in for fully vaccinated individuals compared with 38 percent (24–53 percent) in unvaccinated individuals. Evidence (non-peer reviewed) from the UK has also demonstrated that transmission within a household was reduced by approximately half when the index case was vaccinated with mRNA-CV. Transmission to non-immune individuals in households in Sweden was shown to be significantly reduced and correlated with the proportion of family members vaccinated.

Effectiveness against SARS-CoV-2 Delta variant

Effectiveness of mRNA-CV against symptomatic COVID-19 caused by the Delta variant is reduced in comparison with previous variants (ranging from around 78–93 percent). According to preprint literature, from 7–14 days after two doses, the vaccine remains highly effective against hospitalisation (73–94 percent), severe disease and death (80–97 percent) in a range of groups. The risk of infection with Delta is lower in fully vaccinated compared with unvaccinated individuals (hazard ratio 0.35; 95% CI 0.32–0.39), but some vaccinated individuals may spread infection.

Duration of immunity

There has been insufficient time since the commencement of clinical trials and vaccination campaigns to assess fully how long immunity lasts following immunisation or natural infection. Prior to widespread Delta variant, a gradual decline in vaccine efficacy was observed to 6 months after vaccination to 91.3 percent (95% CI 89–93.2...
percent), but protection against severe disease was maintained (vaccine efficacy of 96.7 percent; 80.3–99.9).\textsuperscript{56} Waning in neutralising antibody levels has been correlated with predominantly mild or asymptomatic breakthrough infections in health care workers.\textsuperscript{57}

**Effectiveness of booster doses**

To prolong protection many countries, including New Zealand, have introduced a booster dose given from six months after the primary course. Booster doses were shown to reduce the rates of COVID-19 by a factor of 11.3 (95% CI 10.4–12.3) and severe illness by a factor of 5.4 (4.8–6.1) in older adults aged from 60 years in Israel.\textsuperscript{58}

**Adenovirus vector COVID-19 vaccine (ChAd-CV) – COVID-19 Vaccine AstraZeneca**

**Efficacy**

The initial data, pooled from four phase III clinical trials conducted in Brazil, South Africa and the UK, showed two doses given four weeks apart, gave ChAd-CV a vaccine efficacy against symptomatic COVID-19 of 62.1 percent (95% CI 41.0–75.7 percent) from 14 days after the second dose.\textsuperscript{59} Another phase III clinical trial in US, Peru and Chile reported an estimated overall vaccine efficacy of 74.0 per cent (95% CI 65.3–80.5) in those aged under 65 years and 83.5 percent (95% CI 54.2–94.1) in those aged 65 years or older from 15 days after two doses given four weeks part. Among 17,662 participants, no cases of severe or critical COVID-19 were seen in the fully vaccinated group compared with eight cases out of 8,550 participants who received placebo (vaccine efficacy of 100 percent [72.2–100]).\textsuperscript{60}

**Effectiveness**

Early data (pre-Delta variant) after the first dose from study conducted in Scotland gave a vaccine effectiveness of 88 percent (95% CI 75–94) against hospital admission 28–34 days post vaccination with the first dose for older adults (median age 65 years).\textsuperscript{61} A significantly protective effect was seen against hospitalisation and death due to COVID-19 from 14 days after the first dose of ChAd-CV or mRNA-CV.\textsuperscript{62} Data is limited about effectiveness against transmission.

**Effectiveness against Delta variant**

A modest reduction in effectiveness after two doses of ChAd-CV against symptomatic disease caused by Delta (67 percent; 95% CI 61–72) compared with Alpha variant (74.5 percent; 68–89) has been reported.\textsuperscript{63} UK Health Security Agency (formerly Public Health England) found the effectiveness against hospitalisation with Delta was 71 percent (51–83) after one dose and 92 percent (75–97) after two doses of ChAd-CV; similar to the vaccine effectiveness against Alpha. The non-peer-reviewed study linked symptomatic COVID-19 cases with hospital admission and vaccine status.\textsuperscript{54}

**Duration of protection**

Limited waning has been observed the UK over nine months since the COVID-19 vaccines were first introduced (non-peer-reviewed data). Vaccine effectiveness was
shown to peak in the early weeks after the second dose but for ChAd-CV effectiveness across all age groups fell to 47.4 percent (95% CI 45–49.6) after 20 weeks against symptomatic disease caused by the Delta variant. Effectiveness against hospitalisation was maintained at 77.0 percent (70.3–82.3) and 78.7 percent (52.7–90.4) against death. The greatest waning was observed (preprint data) in those aged over 65 years and those aged 40–64 years with underlying medical conditions compared with healthy adults.64

Mixed COVID-19 vaccine schedules

Much of the data available around mixed (heterologous) COVID-19 vaccine schedules have investigated ChAd-CV (AstraZeneca) followed by mRNA-CV (Comirnaty) as the second dose (heterologous prime-boost schedules).65, 66 The humoral immune response was found to be stronger with a ChAd/mRNA primary schedule than ChAd/ChAd schedule against different SARS-CoV-2 variants including Delta.65, 67 The T cell response was also found to be higher following heterologous dosing.68 The ComCOV study in the UK found that when ChAd-CV was given 4 weeks after mRNA-CV, the anti-S protein IgG antibody response was lower than homologous mRNA-CV dosing (geometric mean ratio [GMR] 0.51; 95% CI 0.43–∞), but higher than ChAd/ChAd. Giving mRNA-CV after ChAd-CV first dose, produced a higher response than ChAd/ChAd dosing (GMR 9.2; 7.5–∞). Taking age, comorbidity and different immunological outcomes into consideration, the overall humoral response of mRNA/mRNA was favoured over mRNA/ChAd dosing and ChAd/mRNA was favoured over ChAd/ChAd.69

5.4.4 Transport, storage and handling

mRNA COVID-19 vaccine – Comirnaty (Pfizer/BioNTech)

To preserve the integrity of the mRNA in this vaccine, storage at ultra-low temperature freezer (between -90°C and -60°C) is required. At these ultra-low temperatures, the shelf-life is nine months. Trays of unopened vials may be stored and transported at -25°C to -15°C for a total of two weeks on one occasion only. Once an individual vial has been removed from the vial tray, it should be thawed for use.

The vaccine will be thawed in batches, packed into cartons and distributed from the central warehouse. Each carton will have a label with an updated batch number and expiry date and time. Expiry reduces from 6 months to 31 days once thawed. Thawed vaccines will be shipped to vaccination sites as per the standard cold chain distribution process.

Store undiluted vials at +2°C to +8°C for up to 31 days (including up to 12 hours for transportation) including up to two hours at room temperature (up to +30°C). After dilution, store vials between +2°C and +30°C and use within six hours. Any remaining vaccine in the vial must be discarded after six hours. Do not refreeze. See 2021 Addendum to the National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition) (available at health.govt.nz/publication/2021-addendum-national-standards-vaccine-storage-and-transportation-providers-2017-2nd-edition).
Adenovirus vector COVID-19 vaccine (ChAd-CV) – COVID-19 Vaccine AstraZeneca


Store at +2°C to +8°C. Do not freeze. Protect vials from light. Unopened vials have a shelf-life of six months. Once cap has been removed from vial, store in fridge and use within 48 hours. Vaccines should ideally be used within an hour of preparation, however, any doses that are drawn up into syringes must be used within five hours (stored at +2°C to 30°C) or before vial 48-hour expiry is reached, whichever is soonest. To ensure optimum use, in New Zealand, the vaccine is recommended to be always stored in the fridge.

5.4.5 Dosage and administration

mRNA COVID-19 vaccine – Comirnaty (Pfizer/BioNTech)

Each dose of mRNA-CV is 0.3 mL (30 µg) to be administered intramuscularly. Two doses are given at least 21 days apart for individuals aged 12 years or older.

Each multi-dose vial contains 0.45 mL of vaccine and should be diluted with 1.8 mL of 0.9% NaCl. Once diluted, each reconstituted vaccine will supply six (up to seven) doses of 0.3 mL. If the amount of vaccine remaining in the vial cannot provide a full 0.3 mL dose, discard the vial and any excess volume. Do not pool excess vaccine from multiple vials.

An observation period following vaccination of at least 15 minutes is recommended (see section 5.6.2). This is to ensure that any anaphylactic-type reactions can receive prompt treatment.

This vaccine is latex-free. The vial stopper is made with synthetic rubber (bromobutyl), not natural rubber latex.

Preparing mRNA-CV multi-dose vial

Note that the process for drawing up mRNA-CV differs from the recommendations for other multi-dose vial vaccines as described in section A7.2 in Appendix 7. To follow international guidance around the use of low dead space needles, the needle used to draw up mRNA-CV is also used to administer the injection. Unless you plan to administer the vaccine dose immediately, carefully replace the needle guard and place syringe onto a ridged tray for storage, for example, if all six doses are prepared at one go in a mass vaccination setting.

For detailed instructions for mRNA-CV multi-dose vial preparation and administration see the most current IMAC COVID-19 education factsheet ‘Instructions for multi-dose
Adenovirus vector COVID-19 vaccine (ChAd-CV) – COVID-19 Vaccine AstraZeneca

Each dose of ChAd-CV is 0.5 mL to be administered intramuscularly. Two doses are given from 4 to 12 weeks apart for individuals age 18 years or older.

Each multidose vial contains ten doses (total 5 mL). The vials do not require dilution or reconstitution. For detailed instructions for ChAd-CV multidose vial administration see the most current IMAC COVID-19 education factsheet, ‘Preparation of AstraZeneca COVID-19 vaccine’ available from covid.immune.org.nz.

An observation period following vaccination of at least 15 minutes is recommended (see section 5.6.2). This is to ensure that any anaphylactic-type reactions can receive prompt treatment.

This vaccine is latex-free. The vial stopper is made with synthetic rubber (an elastomeric with an aluminium overseal), not natural rubber latex.

Coadministration with other vaccines

Either dose of mRNA-CV or ChAd-CV can be administered at any time before, after or simultaneously with other Schedule vaccines (in separate syringes, at separate sites), including MMR, influenza, HPV, Tdap and meningococcal vaccines. Note: the only exception is the live herpes zoster vaccine (ZV; Zostavax), for which, spacing of at least seven days is recommended before or after mRNA-CV or ChAd-CV. TST/Mantoux testing for tuberculosis can also be conducted at any time before, after or simultaneously with mRNA-CV or ChAd-CV.

5.5 Recommended immunisation schedule

The COVID-19 vaccines were initially only available according to a prioritisation schedule for defined groups, however, since 1 September 2021, all individuals in New Zealand aged from 12 years are eligible to COVID-19 immunisation.

For legal definition of who is considered fully vaccinated against COVID-19 within the New Zealand border see ‘New Zealand definition for fully vaccinated for use inside the border (October 2021)’ available from the Ministry of Health, as agreed by the Director General of Health. See section 5.8.2 for examples of approved vaccination schedules.

Temporary medical exemptions from vaccine mandates for the first or second dose of COVID-19 vaccination, where a suitable appropriate and approved COVID-19 vaccine is available from covid.immune.org.nz.


5.5.1 mRNA COVID-19 vaccine – Comirnaty (Pfizer/BioNTech)

All individuals from the age of 12 years are recommended to receive two doses of mRNA-CV, given at least 21 days after the first dose. Individuals are considered fully vaccinated after completing the full primary course, full immunity develops from around seven days after the second dose.

To date, mRNA-CV has not been approved for use in children aged younger than 12 years in New Zealand. A clinical trial has been conducted in 5–11 year-olds and emergency use approval has been granted in the US. Trials are ongoing in younger age groups.

5.5.2 Adenovirus vector COVID-19 vaccine (ChAd-CV) – COVID-19 Vaccine AstraZeneca

The preferred vaccine for the Schedule is mRNA-CV, however, ChAd-CV can be offered (if not contraindicated, see section 5.6), where available, to individuals who are contraindicated mRNA-CV or have experienced an adverse reaction to the first dose of mRNA-CV. It can also be offered to individuals who have declined mRNA-CV and would prefer an alternative vaccine. Individuals opting for this vaccine are recommended to discuss the benefit and potential risks of receiving this vaccine with a health professional. Written consent is recommended for all ChAd-CV doses.

Where two primary doses of ChAd-CV are given, no prescription is required. In cases where another COVID-19 vaccine was given previously, ChAd-CV given as the second primary or booster dose (see section 5.5.3) is off-label use and will require prescription from an authorised provider (under regulation s25 of the Medicines Act 1981).
5.5.3 Breastfeeding

While lactating women/people were not included in phase III studies, as with all schedule vaccines, there are no safety concerns about giving mRNA-CV or ChAd-CV to lactating women/people.

5.5.4 Pregnancy

mRNA COVID-19 vaccine – Comirnaty (Pfizer/BioNTech)

Women/people who are pregnant are encouraged to be routinely vaccinated with mRNA-CV at any stage of pregnancy. The risk of an adverse outcomes from COVID-19 infection during pregnancy is significantly higher compared to non-pregnant adults (see section 5.2.2)\textsuperscript{30}. Internationally, many women have been given this vaccine while pregnant and safety surveillance data of large numbers of pregnant people indicate that there are no safety concerns with administering mRNA-CV in any stage of pregnancy.\textsuperscript{72} There is also emerging evidence of antibody transfer in cord blood and breast milk which can offer protection to infants through passive immunity.\textsuperscript{73, 74, 75}

Pregnant women/people with questions or concerns are encouraged to discuss them with their health professional. People who are trying to become pregnant do not need to avoid pregnancy after receiving mRNA-CV.

There are no known safety concerns, but due to limited experience, ChAd-CV is not recommended for use in pregnancy – see Precautions (section 5.6.2)

For information about booster doses, see section 5.5.9.

5.5.5 Frail elderly individuals

In general, it is recommended that all eligible adults, including the frail and elderly with comorbidities are offered vaccination against COVID-19, if there are no contraindications (see section 5.6.1) to its administration, to provide protection for the individual as well as their community.

5.5.6 Individuals receiving cardiology care

It is recommended that all individuals aged 12 years or older receive two doses of mRNA-CV given at least 21 days apart. Pre-existing cardiac conditions, in general, are not regarded as precautions or contraindications to vaccination. This includes pre-existing rheumatic heart disease. Note that many cardiac conditions increase the risk from COVID-19 disease. Those with a history of pericarditis or myocarditis, unrelated to mRNA-CV, can have the vaccination if the condition is completely resolved, (ie, no symptoms and no evidence of ongoing cardiac inflammation). See section 5.6.2 for those who have myocarditis associated with mRNA-CV.
ChAd-CV can be offered as an alternative to mRNA-CV, if not contraindicated, from the age of 18 years. Those with a history of myocarditis and pericarditis related to mRNA-CV can be offered ChAd-CV.

5.5.7 Previous history of COVID-19 infection

Vaccination should be offered regardless of an individual's history of symptomatic or asymptomatic SARS-CoV-2 infection. As the duration of protection post infection is currently unknown, vaccination is recommended. Although, there are no specific safety concerns around giving mRNA-CV to individuals with a history of SARS-CoV-2 infection or symptomatic COVID-19, as seen after the second dose of mRNA-CV in SARS-CoV-2 naïve individuals, those who have had previous infection can experience more systemic reactogenicity after the first dose of mRNA-CV (see section 5.7.1). Viral or serological testing is not required before vaccination.

In a person who has had a previous SARS-CoV-2 infection, an individual is considered fully vaccinated after two doses of mRNA-CV (or another COVID-19 vaccine, see section 5.8.2). In these individuals, vaccination is recommended to be given from four weeks after recovery, or four weeks from the first confirmed positive PCR test if asymptomatic, and when cleared to leave isolation by a clinician. This also applies to the second dose for individuals who have SARS-CoV-2 infection after their first dose.

5.5.8 Individual with immunodeficiencies or receiving immunosuppressive agents

There are no safety concerns around administering mRNA-CV or ChAd-CV to individuals who are immunocompromised and/or receiving immunosuppressive agents. As with other non-live vaccines, the antibody response to these vaccines may be reduced and protection may be suboptimal but, it is likely to be adequate to protect against severe disease. It is recommended to discuss the optimal timing for vaccination with a specialist before the vaccine appointment for those who are severely immunocompromised. Ideally, vaccination should be conducted prior to any planned immunosuppression (see section 4.3.7).

It is important that all close contacts of immunocompromised individuals aged from 12 years are fully immunised.

Individuals who are severely immunocompromised

A third primary dose of mRNA-CV is indicated for certain individuals who are severely immunocompromised who are likely to have not responded adequately to the first two doses. Serology is not recommended. This third primary dose is distinct from the booster dose (see section 5.5.9). Individuals who receive this third primary dose are recommended to also be given the booster dose at least six months later.
Preferably, this third dose should be administered at least eight weeks after the second dose. However, the timing also needs to consider current or planned immunosuppressive therapies. If the period of least immunosuppression is less than eight weeks, the vaccination can be given any time from four weeks after dose two. Where possible, delay the third dose until two weeks after the period of immunosuppression (in addition to the clearance time-period of therapeutic). If this is not possible, consider vaccination during a treatment ‘holiday’ or at a nadir of immunosuppression between doses of treatment.

These additional doses are currently considered off label and can only be offered by an authorised prescriber with informed consent (under regulation s25 of the Medicines Act 1981). This is under review with Medsafe. For further guidance see health.govt.nz/our-work/diseases-and-conditions/covid-19-novel-coronavirus/covid-19-vaccines/covid-19-vaccine-information-health-professionals/covid-19-vaccine-policy-statements-and-clinical-guidance.

If a significant adverse reaction to mRNA-CV has occurred that contraindicates further mRNA-CV doses, then ChAd-CV may be given (if not contraindicated).

Table 5.1 provides guidance on types of immunocompromise for which a third primary dose is recommended. For further information on corticosteroid indicative dosages and examples of non-corticosteroid agents considered immunosuppressive, see section below and Table 5.2.

**Table 5.1: Individuals (aged 12 and older) with severe immunocompromise recommended to receive a third primary dose of mRNA-CV**

Note: This list is not exhaustive but provides guidance on scenarios where a third primary dose is recommended. There is variation between individuals in response to immunosuppressive or immunomodulating therapy. Clinicians may use their judgement for conditions or medications that are not listed here that are associated with severe immunocompromise.

<table>
<thead>
<tr>
<th>Eligible group / indication</th>
<th>Treatments or health status</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Individuals with primary or acquired immunodeficiency states at the time of vaccination</strong></td>
<td></td>
</tr>
<tr>
<td>Acute and chronic leukaemia and clinically aggressive lymphomas (including Hodgkin’s lymphoma)</td>
<td>under treatment, or within 12 months of achieving cure or remission</td>
</tr>
<tr>
<td>Chronic lymphoproliferative disorders, including haematological malignancies and plasma cells dyscrasias</td>
<td>under specialist follow up</td>
</tr>
<tr>
<td>Active HIV infection / AIDS</td>
<td>current CD4 count &lt;200 cells/µl</td>
</tr>
<tr>
<td>Primary or acquired cellular and combined immune deficiencies</td>
<td>lymphopenia (&lt;1,000 lymphocytes/µl) or functional lymphocyte disorder.</td>
</tr>
</tbody>
</table>

*Continued overleaf*
### Eligible group / indication

<table>
<thead>
<tr>
<th>Treatments or health status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allogenic or autologous haematopoietic stem cell transplant</td>
</tr>
<tr>
<td>Persistent agammaglobulinaemia due to primary immunodeficiency and secondary to disease/therapy</td>
</tr>
</tbody>
</table>

### Individuals on, or recently on, immunosuppressive therapy at the time of vaccination

<table>
<thead>
<tr>
<th>Treatments or health status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Following a solid organ transplant</td>
</tr>
<tr>
<td>B cell depleting biologic therapy, including rituximab</td>
</tr>
<tr>
<td>Biologics or targeted therapy(^b) for autoimmune or autoinflammatory disease</td>
</tr>
<tr>
<td>Immunosuppressive cytotoxic chemotherapy or immunosuppressive radiotherapy for any indication</td>
</tr>
</tbody>
</table>

### Individuals with chronic immune-mediated inflammatory disease who were receiving or had received immunosuppressive therapy prior to vaccination

<table>
<thead>
<tr>
<th>Treatments or health status</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-dose or long-term moderate dose corticosteroids (for indicative dosages, see below)</td>
</tr>
<tr>
<td>For select immunosuppressant drugs(^b,c)</td>
</tr>
<tr>
<td>Certain combination therapies at where cumulative effect is severely immunosuppressive, as determined by clinical judgment</td>
</tr>
</tbody>
</table>

### Individuals receiving long term haemodialysis or peritoneal dialysis

- **Note**: this list is not exhaustive but provides an indication of conditions where an individual is recommended to receive a third primary dose.

### Individuals receiving corticosteroids

A third primary dose of mRNA-CV is recommended for individuals with chronic immune-mediated inflammatory disease who are receiving or have received high dose or long-term moderate doses of corticosteroids prior to vaccination, for example:

- high dose – equivalent to at least 20 mg prednisolone per day for more than ten days, in previous month
- moderate dose – equivalent to at least 10 mg prednisolone per day for more than four weeks, in previous three months
• also includes for those who received high dose corticosteroids for any reason – equivalent to at least 40 mg per day for more than a week, in the previous month.

Individuals for whom third primary dose is not routinely recommended include those who require:
• brief corticosteroid therapy, for example for asthma, chronic obstructive pulmonary disease or COVID-19 – equivalent to 40mg or less prednisolone per day
• low locally acting corticosteroids, inhaled or topical
• replacement corticosteroid treatment for adrenal insufficiency.

Clinical judgement is required to determine the level of immunosuppression and these dosages are only indicative examples. In some cases, combinations of therapies can have a cumulative effect that is severely immunosuppressive.

Individuals receiving non-corticosteroid immunomodulatory agents

A third primary dose of mRNA-CV is recommended for individuals with chronic immune-mediated inflammatory diseases who were receiving or had received immunosuppressive therapy prior to primary COVID-19 vaccination. Indicative examples are given in Table 5.2. Clinical judgement is required to determine the level of immunosuppression. In some cases, combinations of therapies can have a cumulative effect that is severely immunosuppressive.

Table 5.2: Examples of non-corticosteroid immunosuppressant therapies for which a third primary dose of mRNA-CV is recommended or not routinely recommended

<table>
<thead>
<tr>
<th>Clinicians may use their judgement for conditions or medications that are not listed here that are associated with severe immunocompromise and in some cases based on dosages or combinations of therapies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Examples of non-corticosteroid agents for which a third dose is recommended</td>
</tr>
<tr>
<td><strong>Agent</strong></td>
</tr>
<tr>
<td>Mycophenolate, methotrexate, leflunomide, 6-mercaptopurine</td>
</tr>
<tr>
<td>Thiopurines</td>
</tr>
<tr>
<td>Alkylating agents</td>
</tr>
<tr>
<td>Systemic calcineurin inhibitors</td>
</tr>
<tr>
<td>BTK inhibitors</td>
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<tr>
<td>JAK inhibitors</td>
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<tr>
<td>Sphingosine 1-phosphate receptor modulators</td>
</tr>
<tr>
<td>Anti-CD52 antibodies</td>
</tr>
<tr>
<td>Anti-complement antibodies</td>
</tr>
<tr>
<td>Anti-thymocyte globulin</td>
</tr>
</tbody>
</table>

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Examples of non-corticosteroid agents for which third primary dose is not routine recommended

<table>
<thead>
<tr>
<th>Agent</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-integrins</td>
<td>natalizumab</td>
</tr>
<tr>
<td>Anti-TNF-α antibodies</td>
<td>infliximab, adalimumab, etanercept</td>
</tr>
<tr>
<td>Anti-IL-1 antibodies</td>
<td>anakinra</td>
</tr>
<tr>
<td>Anti-IL-6 antibodies</td>
<td>tocilizumab</td>
</tr>
<tr>
<td>Anti-IL-17 antibodies</td>
<td>secukinumab</td>
</tr>
<tr>
<td>Anti-IL-4 antibodies</td>
<td>dupilumab</td>
</tr>
<tr>
<td>Anti-IL-23 antibodies</td>
<td>ustekinumab</td>
</tr>
</tbody>
</table>

a. For immune checkpoint inhibitors see section 4.3.2

5.5.9 Booster doses

A single dose of mRNA-CV is recommended to be given at least six months after completion of the two-dose primary series to those aged 18 years and above. A booster dose is not currently approved by Medsafe for use in those aged under 18 years.

A booster dose is particularly recommended for those individuals most at risk of exposure to SARS-CoV-2 and those most at risk of serious COVID-19 disease outlined below.

- Frontline healthcare workers, particularly those most likely to be exposed to COVID-19 in the community or in regions where further risk of spread of COVID-19 is high.
- All individuals who are aged 65 years or over.
- Māori and Pacific People aged 50 years and over.
- Anyone aged 18 years or older at increased risk of severe COVID-19:
  - eligible for funded influenza vaccine (See Booster doses in pregnancy)
  - disabled or caring for a person with a disability
  - severely obese (BMI ≥40)
  - hypertension, requiring two or more medications to control
  - adult in a custodial setting
  - have been diagnosed with a severe mental illness (including schizophrenia, major depressive disorder, bipolar disorder or schizoaffective disorder, and adults currently accessing secondary and tertiary mental health and addiction services.

Although mRNA-CV is the preferred vaccine, ChAd-CV can also be used as a booster dose, if not contraindicated. If using ChAd-CV as a booster dose, a prescription from an authorised prescriber is required as it is an off-label use (under regulation s25 of the Medicines Act 1981).
Booster doses in pregnancy

Pregnant women/people aged from 18 years who completed their primary series prior to pregnancy can receive a booster dose of mRNA-CV at any stage of pregnancy (from six months after a primary course). As given above, booster doses are particularly recommended for individuals most at high risk of exposure to SARS-CoV-2 or with significant medical issues that increase their risk for severe COVID-19.

There is currently no evidence to indicate that a booster dose late in pregnancy is required for a person who was fully vaccinated or completed their primary series early in their pregnancy. Generally, this age group has a good immune response to the vaccine and a full primary course completed in pregnancy would be expected to offer sufficient protection throughout the pregnancy.

Individuals who are severely immunosuppressed are recommended to receive three primary doses with the third dose given at least eight weeks after dose two (see section 5.5.8; this is not the same as booster doses). In this case, a further booster is not required in pregnancy but can be given as time-appropriate after delivery, at least six months after completion of their primary series. Pregnant women with significant comorbidities, who are not eligible for a third primary dose, should discuss the timing of their booster dose with a health professional.

5.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

5.6.1 Contraindications

mRNA COVID-19 vaccine – Comirnaty (Pfizer/BioNTech)
A history of anaphylaxis to any component or previous dose of mRNA-CV is a contraindication.

Adenovirus vector COVID-19 vaccine (ChAd-CV) – COVID-19 Vaccine AstraZeneca
A history anaphylaxis to any components or previous dose of ChAd-CV is a contraindication.

A history of major venous and/or arterial thrombosis in combination with thrombocytopenia following vaccination with any COVID-19 vaccine is a contraindication for ChAd-CV.

Individuals with a history of capillary leak syndrome should not receive ChAd-CV.
5.6.2 Precautions

mRNA COVID-19 vaccine – Comirnaty (Pfizer/BioNTech)

A definite history of immediate allergic reaction to any other product is considered as a precaution but not a contraindication to vaccination with mRNA-CV. A slightly increased risk of a severe allergic response in individuals who have had a previous anaphylaxis-type reaction needs to be balanced against the risk of SARS-CoV-2 exposure and severe COVID-19. These individuals can still receive mRNA-CV and observation extended to 30 minutes after vaccination in health care settings, where anaphylaxis can be immediately treated with adrenaline.

When vaccinating an elderly person who has an intercurrent or comorbid condition, ensure they are stabilised or as well as possible before they have the vaccine. Following vaccination ensure good hydration and careful management of potential systemic adverse events, such as fever. It is advisable for them to be with someone else for 24 hours after receipt of the vaccine to help manage potential adverse events.

If myocarditis, myopericarditis or pericarditis occurs after dose one or two of mRNA-CV, defer further doses of mRNA-CV. Give one dose of ChAd-CV (if not contraindicated) once condition has resolved or at least four weeks later (for primary series) and at least six months later for booster dose. Vaccination is not recommended for anyone with current active cardiac inflammation. Seek further advice from IMAC.

Adenovirus vector COVID-19 vaccine (ChAd-CV) – COVID-19 Vaccine AstraZeneca

Thrombosis with thrombocytopenia syndrome

A rare but increased risk of thrombosis with thrombocytopenia syndrome (TTS) has been identified with adenoviral vector vaccines including ChAd-CV, typically occurring within 3 weeks of vaccination and more prevalent in younger adults (<50 years). Vaccinated individuals should seek immediate medical attention if they develop symptoms such as a severe or persistent headache, blurred vision, confusion, seizures, shortness of breath, chest pain, leg swelling, leg pain, persistent abdominal pain or unusual skin bruising and or petechiae after vaccination.

Individuals with diagnosed thrombosis within 21 days of vaccination with ChAd-CV should be investigated for thrombocytopenia. Similarly, those diagnosed with thrombocytopenia within 21 days of vaccination should be actively investigated for signs of thrombosis; if thrombosis is excluded, consider a diagnosis of vaccine-induced immune thrombocytopenia (ITP).

It is recommended that individuals with a history of thromboses, certain procoagulant autoimmune disorders or thrombocytopenia discuss the benefits and risks of vaccination with a health professional or specialist as they remain at risk of recurrent thromboses due to COVID-19.
The specific risks for TTS have not been identified. Individuals with a history of the following rare causes of thrombosis are not advised to receive ChAd-CV:

- cerebral venous sinus thrombosis (CVST)
- idiopathic thrombosis in the abdomen such as in splanchnic circulation, including mesenteric, portal or splenic veins
- heparin-induced thrombocytopenia
- antiphospholipid syndrome with thrombosis.

**Pregnancy**

There is insufficient safety data to recommend ChAd-CV for use during pregnancy, pregnant women/people are advised to discuss the benefit and potential risks of receiving this vaccine in pregnancy with their health professional. There are no safety concerns should it be given inadvertently in pregnancy.

### 5.7 Potential responses and AEFIs

#### 5.7.1 Potential responses

**mRNA COVID-19 vaccine – Comirnaty (Pfizer/BioNTech)**

Commonly reported responses to mRNA-CV (during clinical trials and post-licensure) are injection-site pain, headache and fatigue; other responses included muscle aches, feeling generally unwell, chills, fever, joint pain and nausea. These occurred most often after dose two and in younger adults (aged 18–55 years), and within one or two days of vaccination. Most are mild or moderate in severity and are self-limiting.\(^{48,77}\) Analgesia, such as paracetamol or ibuprofen (as appropriate), can be taken for pain and discomfort following vaccination. It is advisable to limit vigorous exercise if feeling unwell.

**Adenovirus vector COVID-19 vaccine (ChAd-CV): COVID-19 Vaccine AstraZeneca**

Commonly reported responses to ChAd-CV (during clinical trials and post-licensure) are similar to mRNA-CV, including injection-site pain, headache and fatigue; other responses included muscle aches, feeling generally unwell, chills, fever, joint pain and nausea. These occurred most often after dose one and in younger adults (aged 18–55 years), and within one or two days of vaccination.\(^{59,78}\) Most are mild or moderate in severity and are self-limiting. Adverse reactions were generally milder and reported less frequently after dose two or a third dose.\(^{79}\)
Breast screening and CT scans

Transient unilateral axillary adenopathy, a known response to vaccination, is particularly noted following vaccination with mRNA-CV due to the scale of the roll-out and age groups being immunised. Early estimates suggest that 12–16 percent of vaccine recipients experience axillary adenopathy after vaccination with mRNA-CV, starting one or two days after vaccination and which can persist for at least two weeks.80

When attending breast screening and mammography appointments, it is recommended that individuals advise the radiographer or doctor that they have received a COVID-19 vaccine recently. It is advised to monitor any lymph node changes that persist for longer than six weeks after vaccination.80

Likewise, individuals undergoing FDG PET/CT scans for cancer screening are advised to inform the radiologist or their oncologist that they have been recently vaccinated, or, if possible, to have COVID-19 vaccination at least two weeks before a scheduled scan or as soon as possible afterwards. Treatment should not be delayed.

5.7.2 AEFIs

Adverse events following immunisation (AEFIs) with the COVID-19 vaccines are being closely monitored during clinical trials and by post marketing surveillance. A dedicated COVID-19 vaccine AEFI reporting tool is available online from CARM (see section 1.6.3). Medsafe reports weekly on the AEFI reported to CARM after COVID-19 vaccinations (see medsafe.govt.nz/COVID-19/vaccine-report-overview.asp).

A list of adverse events of special interest (AESIs), including those previously associated with immunisation in general and with the particular vaccine platforms, was created by Safety Platform for Emergency Vaccines (SPEAC) in collaboration with the Coalition for Epidemic Preparedness Innovations (CEPI) and based on existing and new Brighton Collaboration case definitions. For further information, see brightoncollaboration.us/covid-19. Global pharmacovigilance and active safety monitoring systems continue to watch for both AESI and unexpected AEFI.

mRNA COVID-19 vaccine – Comirnaty (Pfizer/BioNTech)

As of 30 August 2021, overall, no AESI signals had been detected by the Vaccine Safety Datalink in the US up to 21 days after vaccination, following the administration of over 13 million doses of mRNA-CV (Comirnaty), however, subgroup analyses did find mRNA-CV to be associated with a slight increase in myocarditis and pericarditis in younger people (aged under 30 years).81,82

Preliminary phase II/III clinical trial safety data reported lymphadenopathy in 64 (0.3%) vaccine recipients and six (<0.1%) placebo recipients (follow-up of up to 14 weeks after second dose of a subset of 18,860 participants who received at least one dose of mRNA-CV). Four vaccine-related adverse events were recorded (namely, shoulder injury related to vaccine administration, lymphadenopathy local to injection site, paroxysmal ventricular arrhythmia and right leg paraesthesia). No deaths were related
to either the vaccine or the placebo. During clinical trial follow-up to 1 February 2021, acute peripheral facial paralysis (Bell’s palsy) was reported by four vaccinated participants and none in the placebo group. No safety signal has been detected for this condition as an AESI, and safety monitoring is ongoing.

Myocarditis and pericarditis

A small increase in incidence of myocarditis, myopericarditis and pericarditis has been observed following the second dose of mRNA-CV vaccination (40.6 cases per million doses in young males and 4.2 cases per million in young females, aged 12-29 years, decreasing to 2.4 and 1.0 per million, respectively, in men and women aged over 30 years). Most cases occur within 14 days of vaccination. A review of clinical records in the US observed the median time to onset for myocarditis was 3.5 days (interquartile range 3.0–10.8 days) after vaccination and a median of 20 days (range 6.0–41 days) for pericarditis. These cases have typically been mild with full recovery after standard treatment and rest.

Myocarditis and pericarditis are uncommon conditions considered to be associated with viral infection, including COVID-19. Recently vaccinated individuals should seek immediate medical attention if they experience new onset of (acute and persisting) chest pain, shortness of breath or arrhythmia (palpitations). Diagnosis is based on elevated troponin, C-reactive protein and electrocardiogram and/or MRI findings. Report all cases to CARM as Medsafe continues to monitor this AEFI closely. Defer the second dose if myocarditis occurs after the first dose of mRNA-CV and seek advice from IMAC.

Anaphylaxis

Following approval for use in the US, the VAERS detected 47 cases of anaphylaxis after administration of just under ten million doses (around five cases per million doses) mRNA-CV (Pfizer/BioNTech). The median interval to symptom onset was ten minutes (range <1–1140 minutes), almost 90 percent occurred within 30 minutes of vaccination. All were successfully treated with adrenaline. See section 5.6 for contraindications and precautions.

Frail elderly

A follow-up, after approximately two million doses of mRNA-CV were delivered through long-term residential care facilities to elderly and frail residents in the US found no increase in deaths post vaccination. Deaths were to be expected and consistent with the all-cause mortality rate and causes of death for these individuals, who have multiple comorbidities, declining health and require end-of-life care. There are no added safety concerns about the use of this vaccine in the elderly.
Adenovirus vector COVID-19 vaccine (ChAd-CV): COVID-19 Vaccine AstraZeneca

Thrombosis with thrombocytopenia syndrome

Adenoviral vector COVID-19 vaccines, including ChAd-CV (AstraZeneca), have been linked to a rare, newly identified condition called thrombosis with thrombocytopenia syndrome (TTS; also known as vaccine-induced immune thrombotic thrombocytopenia, VITT). This condition involves blood clotting in various sites, including the brain and abdomen, with thrombocytopenia (depletion of platelets in the blood). Onset occurs around 4 to 30 days after vaccination and is associated with younger age (under 60 years). The pathogenesis of this condition resembles heparin-induced thrombocytopenia (HIT) and differs from the coagulation cascade activation seen during the immune response to SARS-CoV-2 infection.88, 89

As of 11 November 2021, in Australia, the overall incidence of TTS is estimated to be 2 per 100,000 vaccinated and higher for those aged under 60 years (two to three cases per 100,000) after the first dose of ChAd-CV and much lower after the second dose (0.4 per 100,000). Cases after the first dose in young age groups tend to be more serious with clots in unusual location such as brain and abdomen; whereas cases after second doses tend to be older with clots in common locations such as legs and lungs.90 Similarly, in the UK as of 3 November 2021, the incidence of AEFI reports for TTS was after the first dose was 20.1 per million in those aged 18-49 years and 10.9 in those aged 50 and over. The incidence after the second dose was 1.9 cases per million doses and more frequent in older rather than younger age groups. There is no indication of an increased risk of these events after a second dose in any age group. Such that, second dose can be offered those who did not experience TTS after the first dose.91

Immune thrombocytopenia

Cases of suspected immune thrombocytopenia (ITP, also known as idiopathic thrombocytopenic purpura) have been reported following vaccination with ChAd-CV. Fewer than one case per 100,000 vaccinations has been reported in Australia to date.90 Many cases are mild but about 5 percent develop severe bleeding. Cases have extremely low platelet count and signs of thrombocytopenia, which may include unusual bruising, a nosebleed and/or blood blisters in the mouth, and no evidence of thrombosis.

Capillary leak syndrome

Very rare cases of capillary leak syndrome have been reported following vaccination with viral vector vaccines, which appear more apparent in those who have had previous episodes of capillary leak syndrome. This is an extremely rare relapsing-remitting condition and triggers for relapses are not well understood.

Guillain-Barré Syndrome

There is a possible, rare association with the ChAd-CV vaccine and Guillain-Barré syndrome (GBS). Like other infections, GBS has been reported as a potential complication of COVID-19.92, 93 A causal link to the vaccine is still under investigation. Advise those receiving COVID-19 vaccination to seek medical attention if they
experience symptoms that could suggest GBS early as medical care can reduce severity and improve outcomes. Symptoms include weakness and paralysis in the hands or feet that can progress to the chest and face over a few days or weeks.

5.8 Public health measures

There is an ongoing COVID-19 pandemic globally. New Zealand has implemented strict pandemic response control measures to prevent the spread of SARS-CoV-2 in the community. New Zealand has a four-level alert system to stipulate the measures that the whole population needs to take (as described at covid19.govt.nz).

All individuals with symptoms of COVID-19 are expected to seek medical advice and be tested for infection. Rapid contract tracing and nasopharyngeal testing continue to be fundamental components of the public health measures.

Immunisation using COVID-19 vaccines is part of the public health strategy aimed at reducing the risk of transmission of SARS-CoV-2 in the community to below an R₀ of 1 and to reduce the severity of disease and minimise the burden on the health care system in the event of a community outbreak.

Further immunisation measures are likely to be implemented as other vaccines become available.

5.8.1 Post-exposure prophylaxis and outbreak control

Currently, there is no information on the use of mRNA-CV for post-exposure prophylaxis or outbreak control.

5.8.2 Criteria for being considered fully vaccinated in New Zealand against COVID-19

Individuals who have had one dose of mRNA-CV should receive a second dose of the same mRNA-CV to complete the vaccination course (unless contraindicated). Since there is currently no maximum duration between doses one and two of mRNA-CV, it is not indicated to restart the course or to give a third dose. (except in cases of severe immunocompromise, see section 5.5.8).

Data is limited on the interchangeability between COVID-19 vaccines. It is preferable, where possible, to complete the course with the same vaccine. Generally, in cases where one dose of any two-dose COVID-19 vaccine has been given outside of New Zealand, one dose of mRNA-CV is recommended at least four weeks after the first vaccine dose.
Those who have a documented and appropriately completed course of a vaccine approved by Medsafe or World Health Organization Emergency Use Listing (WHO EUL) are considered fully vaccinated and require no further primary dose of mRNA-CV.

The New Zealand definition for fully vaccinated for use inside the border (October 2021) applies from the point of administration of the last dose for an accepted primary vaccination schedule as given in Table 5.3. There is no maximum time limit since the last dose. These definitions can differ for young people aged under 18 years. For mandates and issuing of vaccination certificates (domestic and internationally), check details with employer and Ministry of Health guidance. Individuals participating in registered COVID-19 vaccine clinical trials (as listed at trialsearch.who.int) can apply for temporary exemption (see section 5.8.3).

Table 5.3: Criteria for the definition of fully vaccinated for use within the New Zealand border and additional vaccination requirements.

Further changes to these criteria are likely, check the Ministry of Health COVID-19 website for the most up to date policies.

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Vaccination received / required</th>
<th>Additional requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medsafe or WHO EUL(^a) approved vaccines</td>
<td>Approved number of doses or two doses of any combination (heterologous) schedule(^a)</td>
<td>None</td>
</tr>
<tr>
<td>Any other vaccine authorised by at least 1 government or other authority(^b)</td>
<td>Completed primary course</td>
<td>Plus one dose of a Medsafe approved vaccine, given at least 28 days after previous vaccine dose</td>
</tr>
<tr>
<td>Any other vaccine authorised by at least 1 government or other authority(^b)</td>
<td>Single dose</td>
<td>Plus one dose of a Medsafe approved vaccine, given at least 28 days after previous vaccine dose</td>
</tr>
</tbody>
</table>

\(a\). WHO Emergency Use Listing approved vaccines, including Sinopharm (BIBP), Coronovac (Sinovac), Covishield (AstraZeneca/Serum Institute of India) and Covaxin (Bharat Biotech).

\(b\). See covid19.trackvaccines.org/vaccines/approved

\(c\). Spikevax (Moderna) is also acceptable as an additional dose, where given outside of New Zealand.

For border workers, health and education sector worker (as per the COVID-19 Public Health Response [Vaccinations] Order 2021) who have been vaccinated previously with one dose of Ad26-CV (Janssen), the recommendation is that one dose of mRNA-CV should also be offered at least four weeks later.

Although not required to meet the definition of fully vaccinated, it is recommended to offer another dose of a vaccine approved by Medsafe to those who have had a single dose of Ad26-CV (Janssen) vaccine, particularly those at high risk of serious disease or occupational exposure, to increase protection against infection.
5.8.3 Temporary medical exemptions

Overall, the number of people in New Zealand estimated to be eligible for medical exemptions for COVID-19 vaccination is expected to be small. There are very few situations where a vaccine is contraindicated, and as such, a medical exemption is expected to be rarely required. In some cases, vaccinations may be temporarily deferred due to some acute major medical conditions (major surgery or hospital admission for serious illness).

A vaccination may reasonably be deferred for individuals with some acute major medical conditions, such undergoing major surgery or hospital admission for a serious illness. Typically, these are time-limited conditions, and where a temporary exemption is considered appropriate, should be discussed with general practitioner, IMAC clinical advisory service or a relevant medical specialist.

- Exemptions are only to be given where a suitable alternative COVID-19 vaccine is not readily available for the individual.
- Exemptions should be for a specified time (up to a maximum of six months), for example, reflecting recovery from clinical conditions or pending the availability of alternative vaccines.
- It is likely that most people who are not medically exempt can be safely vaccinated, with some requiring extra care or precautions.

If the individual meets the strict clinical criteria for vaccination exemption, the doctor or nurse practitioner is required to apply to the Director-General of Health and temporary exemption to be decided by the ‘temporary medical exemption panel’. For clinical guidance and further information on applying for temporary medical exemptions, see health.govt.nz/our-work/diseases-and-conditions/covid-19-novel-coronavirus/covid-19-response-planning/covid-19-mandatory-vaccinations/covid-19-exemptions-and-exceptions-mandatory-vaccination.

If a serious adverse event to a previous dose of a COVID-19 vaccine is used as a reason for the exemption, then this may require discussion with the individual’s GP, IMAC clinical advisory service, or relevant medical specialist, if indicated. These reactions do not include common expected local or systemic reactions known to occur within the first few days after vaccination. Examples of serious AEFIs may include: a medically significant illness (eg, myocarditis), potentially life-threatening events (eg, anaphylaxis), severe myalgic encephalomyelitis/chronic fatigue syndrome (ME/CSF) or persistent or significant disability (eg, Guillain-Barré syndrome). See section 5.7.2 for further information on AEFIs.

Those who are not medically exempt from vaccination, include:

- people who had an otherwise negative experience with other vaccines in the past, that is not mentioned above
- disabled people once adequate resources are available to support safe delivery. People with disabilities are generally at higher risk from COVID-19, and therefore are a priority for vaccination
• pregnant people. Pregnancy is not a valid reason for exemption in the absence of any of the criteria listed in the above table. Pregnancy is associated with higher risk from COVID-19 compared to the general population and therefore this group are a priority for vaccination.

5.9 Variations from the vaccine data sheet

The maximum allowance for ChAd-CV storage at room temperature is reduced from 6 hours, as on the datasheet, to a maximum of 5 hours to take into account the time it takes to remove the vial from the fridge and vaccine drawn up. It is recommended that ChAd-CV always to be stored in the fridge (between +2 to +8°C).

References


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