Third Primary Dose of the Pfizer/BioNTech Vaccine Policy Statement and Clinical Guidance

New Zealand COVID-19 Vaccine and Immunisation Programme

Version 3.0

New Zealand Government

MINISTRY OF HEALTH
MANATŪ HAUORA

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Introduction

COVID-19 vaccines are being rolled out in Aotearoa New Zealand through the COVID-19 Vaccine and Immunisation Programme (Programme) overseen by the Ministry of Health (Ministry). This is the country's largest ever immunisation programme.

The Programme offers free COVID-19 vaccinations to everyone within the approved age range. To ensure that the Programme aligns with international evidence, the COVID-19 Vaccine Technical Advisory Group (CV TAG) continuously reviews evidence and provides advice to the Programme.

Background and context

CV TAG provided recommendations on the use of an additional third dose of the Pfizer/BioNTech (Pfizer) vaccine for those who are severely immunocompromised. It is evident that some severely immunocompromised people do not mount a sufficient immune response to provide adequate protection against COVID-19. Severely immunocompromised consumers are also at higher risk of poor health outcomes from COVID-19 compared to non-immunocompromised consumers. This group also tends to have a prolonged infection and viral shedding period, are at higher risk of developing a new variant, and are more likely to transmit the virus to any contacts compared to non-immunocompromised consumers.

Emerging evidence shows that a third dose of the Pfizer/BioNTech vaccine may increase antibody titres in immunocompromised consumers who developed low or no antibody titres to the standard two-dose regimen. Additionally, adverse reactions reported following a third dose are similar to those after a second dose for example, fatigue and pain at injection site and most were reported as mild to moderate.

People who are severely immunocompromised may have a suboptimal immune response to vaccination and should be counselled to continue to follow other public health measures, such as physical distancing, wearing a face covering, practicing hand hygiene, and isolation or quarantine as advised by public health authorities.

Purpose

To provide a policy statement on the administration of a third Pfizer/BioNTech vaccine for severely immunocompromised consumers.

The policy statement and objectives in this document align with the recommendation from the CV TAG. This policy statement should be used alongside the Immunisation Handbook 2020 and the COVID-19 Vaccine and Immunisation Programme Operating Guidelines.

Policy Statement

The Ministry of Heath recommends that consumers with severe immunocompromise be offered a third primary dose of the Pfizer/BioNTech vaccine.

The third primary dose is distinguished from a booster dose. Those aged over 18 who are immunocompromised and have received a third primary dose of a COVID-19 vaccine should only receive a booster dose 6 months after completion of their primary course (ie, 6 months after their third dose). The booster dose can be spaced strategically to allow for optimal dosing in the immunocompromised.

Note 1: This policy statement is specific to the **Pfizer/BioNTech** vaccine, this is the preferred vaccine in Aotearoa New Zealand for the third primary dose. AstraZeneca can be used for the third dose if a significant adverse reaction has occurred after a previous mRNA vaccine dose which contraindicates further doses of mRNA vaccine (eg, anaphylaxis, myocarditis). Advice is available from the Immunisation Advisory Centre (IMAC) for clinicians considering this for their consumers.

Note 2: The third primary dose must be prescribed by a medical practitioner or Nurse Practitioner, in accordance with Section 25 of The Medicines Act 1981, as it is considered off label use, and informed consent must be obtained prior to administration.

Eligibility Criteria

All individuals aged 12 years and over who are severely immunocompromised should be offered a third primary dose of the Pfizer vaccine.

The updated clinical guidance on individuals who should be offered a third primary dose of the Pfizer COVID-19 vaccine is provided in **Appendix 1**. The list is not exhaustive but provides guidance on scenarios where a consumer should receive a third primary dose. The list may expand or be modified over time as more evidence emerges. Advice for clinicians on the guidance is available through the Immunisation Advisory Centre, and this information will be updated periodically through the Immunisation Handbook.

Clinical judgement should be applied by the prescriber to determine whether a third primary dose is required for conditions or medicines that are not listed that are associated with severe immunocompromise.

Pfizer is the preferred vaccine in New Zealand for the third primary dose. AstraZeneca can be used for the third dose if a significant adverse reaction has occurred after a previous mRNA vaccine dose which contraindicates further doses of mRNA vaccine (eg, anaphylaxis, myocarditis).

Dose interval

Dose interval details are provided in **Appendix 1.**

Appendix 1

Updated guidance on individuals who should be offered a third primary dose of the Pfizer COVID-19 vaccine

Note: This list has been updated based on the recent ATAGI guidance. It is not exhaustive but provides guidance on scenarios where a consumer should receive a third primary dose. Drug dose, disease activity, and co-morbidity can affect the severity of immunocompromise. The list may expand or be modified over time as more evidence emerges. Advice for clinicians on the guidance is available through the Immunisation Advisory Centre, and this information will be updated periodically through the Immunisation Handbook.

- Clinical judgement should be applied by the prescriber to determine whether a third primary dose is required for conditions or medicines that are not listed below that are associated with severe immunocompromise.
- Conversely, clinicians may decide that individual patients with conditions or medicines listed below are at low risk of being severely immunocompromised and do not require a third primary vaccine dose.

1. Individuals with primary or acquired immunodeficiency states at the time of vaccination due to conditions including but not limited to (see note above):
    a. acute and chronic leukaemias, and clinically aggressive lymphomas (including Hodgkin's lymphoma) who were under treatment or within 12 months of achieving cure.
    b. individuals under follow up for chronic lymphoproliferative disorders including haematological malignancies such as indolent lymphoma, chronic lymphoid leukaemia, myeloma, Waldenstrom's macroglobulinemia and other plasma cell dyscrasias.
    c. immunosuppression due to HIV/AIDS with a current CD4 count of <200 cells/µl for adults or children 12 years of age and over.
    d. primary or acquired cellular and combined immune deficiencies – those with lymphopaenia (<109 lymphocytes/L) or with a functional lymphocyte disorder.

e. those who had received an allogeneic (cells from a donor) or an autologous (using their own cells) stem cell transplant in the previous 24 months.

f. those who had received a stem cell transplant more than 24 months ago but had ongoing immunosuppression or graft versus host disease (GVHD).

g. persistent agammaglobulinaemia (IgG <3g/L) due to primary immunodeficiency (for example, common variable immunodeficiency) or secondary to disease/therapy.

2. Individuals on, or recently on, immunosuppressive therapy at the time of vaccination including but not limited to (see note above): a.

   a. receiving immunosuppressive therapy for a solid organ transplant.

   b. received within the previous 6 months rituximab or other B cell-depleting biologic therapy for autoimmune or autoinflammatory disease.

   c. received within the previous 3 months other biologics or targeted therapy for autoimmune or autoinflammatory disease. Examples are provided in **Table 1** and are based on the ATAGI list. Clinicians may use their judgement for medicines which are not listed.

   d. received within the previous 6 months cytotoxic chemotherapy or immunosuppressive radiotherapy for any indication.

3. Individuals with chronic immune-mediated inflammatory disease who were receiving or had received immunosuppressive therapy prior to vaccination including but not limited to (see note above):

   a. high dose or long-term moderate dose corticosteroids. Indicative dosage thresholds are provided in **Table 2**.

   b. immunosuppressants:

      i. including mycophenolate, methotrexate, leflunomide, thiopurines (e.g., azathioprine), 6-mercaptopurine, alkylating agents (e.g., cyclophosphamide, chlorambucil), and systemic calcineurin inhibitors (e.g., cyclosporin, tacrolimus). Clinical judgement should be applied by the prescriber to determine whether a third primary dose is required.

      ii. excluding hydroxychloroquine, sulfasalazine, or mesalazine, when used as monotherapy.

c. combinations of immunosuppressive therapy where the cumulative effect is considered to be severely immunosuppressive, as determined by clinical judgement.

4. Individuals receiving long term haemodialysis or peritoneal dialysis should be offered a third primary dose of the Pfizer COVID-19 vaccine.

Table 1: Examples of immunotherapies

A third primary dose is recommended for people taking the following biologics:	
Class	**Examples**
Anti CD 20 antibodies	rituximab, obinutuzumab, ocrelizumab
BTK inhibitors	ibrutinib
JAK inhibitors	ruxolitinib
Sphingosine 1-phosphate receptor modulators	fingolimod
Anti-CD52 antibodies	alemtuzumab
Anti-complement antibodies	eculizumab
Anti-thymocyte globulin	anti-thymocyte globulin

A third primary dose is not routinely recommended for people taking the following biologics*	
Anti-integrins	natalizumab
Anti-TNF-α antibodies	infliximab, adalimumab, etanercept
Anti-IL1 antibodies	anakinra
Anti-IL6 antibodies	tocilizumab
Anti-IL17 antibodies	secukinumab
Anti-IL4 antibodies	dupilumab
Anti-IL23 antibodies	ustekinumab

Immune checkpoint inhibitors	nivolumab, pembrolizumab, ipilimumab, atezolizumab

*A third primary dose is recommended for people taking multiple immunosuppressant medications where the cumulative effect is severely immunosuppressive.

Table 2: Indicative dosage thresholds for corticosteroids

A third primary dose **is recommended** for
a. Individuals with chronic immune-mediated inflammatory disease: i. on high dose corticosteroids (equivalent to ≥20mg prednisone per day for more than 10 days, in the previous month) ii. on long-term moderate dose corticosteroids (equivalent to ≥10mg prednisone per day for more than 4 weeks, in the previous 3 months) b. Individuals who had received high-dose steroids (equivalent to >40mg prednisone per day for more than a week) for any reason, in the previous month
A third primary dose **is not routinely recommended** for:
a. Individuals who had received brief immunosuppression (equivalent to ≤40 mg prednisone per day), for example, asthma / chronic obstructive pulmonary disease / COVID-19) b. Individuals receiving low dose locally acting steroids (inhaled or topical) c. Individuals on replacement corticosteroids for adrenal insufficiency

Dose Interval

The third primary dose of Pfizer should be administered from 8 weeks after the second dose but can be administered as early as 4 weeks after the second dose after consideration of current or planned immunosuppressive therapies.

For time limited immunosuppressive treatment, where possible the dose should be delayed until 2 weeks after the period of immunosuppression, in addition to the time period for clearance of the therapeutic agent.

For long term immunosuppressive treatment, consideration should be given to vaccination during a treatment 'holiday' or at a nadir of immunosuppression between doses of treatment.

References

Ministry of Health. 2020. Immunisation Handbook. Wellington: Ministry of Health. Available from: https://www.health.govt.nz/publication/immunisation-handbook-2020

Ministry of Health. 2021. COVID-19 Vaccine Operating Guidelines. Wellington: Ministry of Health. Available from: https://www.health.govt.nz/our-work/diseases-and-conditions/covid-19-novel-coronavirus/covid-19-vaccines/covid-19-vaccine-information-health-professionals/covid-19-vaccine-operating-and-planning-guidelines#operate

Centers for Disease Control and Prevention (CDC). Science Brief: COVID-19 Vaccines and Vaccination. July 27, 2021; Available from: https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/fullyvaccinated-people.html.

Centers for Disease Control and Prevention (CDC). People with Certain Medical Conditions. 2021; Available from: https://www.cdc.gov/coronavirus/2019ncov/need-extra-precautions/people-with-medical-conditions.html.

UK Government. Joint Committee on Vaccination and Immunisation: advice on priority groups for COVID-19 vaccination. 30 December 2020; Available from: https://www.gov.uk/government/publications/priority-groups-for-coronaviruscovid-19-vaccination-advice-from-the-jcvi-30-december-2020/joint-committeeon-vaccination-and-immunisation-advice-on-priority-groups-for-covid-19vaccination-30-december-2020.

Oliver, S. Data and clinical considerations for additional doses in immunocompromised people. July 22, 2021; Available from: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-07/07COVID-Oliver-508.pdf.

Tenforde, M.W., et al., Effectiveness of SARS-CoV-2 mRNA Vaccines for Preventing Covid-19 Hospitalizations in the United States. medRxiv, 2021: p. 2021.07.08.21259776.

Brosh-Nissimov, T., et al., BNT162b2 vaccine breakthrough: clinical characteristics of 152 fully vaccinated hospitalized COVID-19 patients in Israel. Clinical Microbiology and Infection, 2021.

Centers for Disease Control and Prevention (CDC). COVID-19 Vaccines for

Moderately to Severely Immunocompromised People. August 27, 2021; Available from: https://www.cdc.gov/coronavirus/2019ncov/vaccines/recommendations/immuno.html.

Kamar, N., et al., Three Doses of an mRNA Covid-19 Vaccine in Solid-Organ Transplant Recipients. The New England journal of medicine, 2021. 385(7): p. 661-662.

Longlune, N., et al., High immunogenicity of a messenger RNA-based vaccine against SARS-CoV-2 in chronic dialysis patients. Nephrology Dialysis Transplantation, 2021.

US Food and Drug Administration. FDA Authorizes Additional Vaccine Dose for Certain Immunocompromised Individuals. August 12, 2021; Available from: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19update-fda-authorizes-additional-vaccine-dose-certain-immunocompromised.

PHE. JCVI issues advice on third dose vaccination for severely immunosuppressed.

Press release: vaccinations for coronavirus 2021 01 September 2021 [cited 2021 10 September 2021]; Available from: https://www.gov.uk/government/news/jcviissues-advice-on-third-dose-vaccination-for-severely-immunosuppressed.

JCVI. Updated JCVI guidance for vaccinating immunosuppressed individuals with a third primary dose. 2021 02 September 2021 [cited 2021 12 September]; Available from: https://www.england.nhs.uk/coronavirus/wpcontent/uploads/sites/52/2021/09/C1399-Updated-JCVI-guidance-forvaccinating-immunosuppressed-individuals-with-third-primary-dose.pdf.

JCVI. Independent report: Joint Committee on Vaccination and Immunisation (JCVI) advice on third primary dose vaccination. Independent report 2021 01 September [cited 2021 12 September]; Available from: https://www.gov.uk/government/publications/third-primary-covid-19-vaccinedose-for-people-who-are-immunosuppressed-jcvi-advice/joint-committee-onvaccination-and-immunisation-jcvi-advice-on-third-primary-dosevaccination#advice.