Memo

Third Primary Pfizer mRNA COVID-19 vaccine dose in the immunocompromised: COVID-19 Vaccine Technical Advisory Group (CV TAG) Updated recommendations

Date:	17 November 2021
To:	Joanne Gibbs, Director of National Operations, COVID Vaccine Immunisation Programme
From:	Dr Ian Town, Chief Science Advisor
For your:	Consideration

Purpose of report

1. To summarise the COVID-19 Vaccine Technical Advisory Group's (CV TAG) updated recommendations on the use of a third primary Pfizer mRNA COVID-19 vaccine dose in those who are severely immunocompromised.

Background and context

2. On 21 September 2021, CV TAG issued recommendations for a third primary Pfizer mRNA COVID-19 vaccine dose in the immunocompromised. CV TAG recommended that:
    a. Those with severe immunocompromise be offered an additional dose of the Pfizer vaccine. The list of eligible individuals is taken from the one developed by the UK's Joint Committee on Vaccination and Immunisation (JCVI).[1]
    b. The additional dose should be administered more than 8 weeks after the second dose, with special attention paid to current or planned immunosuppressive therapies. Where possible, the third primary dose should be delayed until 2 weeks after the period of immunosuppression, in addition to the time period for clearance of the therapeutic agent. If not possible, consideration should be given to vaccination during a treatment 'holiday' or at a nadir of immunosuppression between doses of treatment.
    c. The administration of an additional dose is covered by s25 of The Medicines Act 1981, and as such, should only be offered by an authorised prescriber with informed consent from the consumer.
    d. The standard two-dose course of vaccine should be offered to any eligible unvaccinated household contacts aged 12 and over, of immunocompromised individuals.
3. Since then, the Australian Technical Advisory Group on Immunisation (ATAGI) issued updated guidance on the use of a third primary dose of COVID-19 vaccine in individuals who are severely immunocompromised.[2]

4. The Ministry has also received requests for a revised list of individuals from rheumatologists, haematologists, and gastroenterologists.

5. Accordingly, CV TAG met on 9 November 2021 to update recommendations for the use of a third primary Pfizer COVID-19 vaccine dose in the immunocompromised, based on the recently released ATAGI guidance.

Recommendations

6. CV TAG recommend that:

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

        i. The updated 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.

        ii. 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.

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

        i. 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.

        ii. For long term immunosuppressive treatment, consideration should be given to vaccination during a treatment 'holiday'.

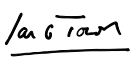
    c. Pfizer is the preferred vaccine in New Zealand for the third primary dose. AstraZeneca can be used for the third dose if a significant adverse reaction has occurred after a previous mRNA vaccine dose which contraindicates further doses of mRNA vaccine (e.g. anaphylaxis, myocarditis).

    d. The administration of a third primary dose is covered by s25 of The Medicines Act 1981, and as such, should only be offered by an authorised prescriber with informed consent from the consumer.

    e. The third primary dose should be distinguished from the 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 (i.e., 6 months after their third dose). The booster dose can be spaced strategically to allow for optimal dosing in the immunocompromised.

    f. The standard two-dose course of vaccine should be offered to any eligible unvaccinated household contacts (aged 12 and over) of immunocompromised individuals.

7. CV TAG will continue to monitor all relevant information and will update their recommendations as further evidence becomes available.



Dr Ian Town

Chief Science Advisor and

Chair of the COVID-19 Vaccine Technical Advisory Group

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 ($<10^9$ 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. 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 for biologics

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 immunosuppressants where the cumulative effect is considered to be 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

References

1. 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/wp-content/uploads/sites/52/2021/09/C1399-Updated-JCVI-guidance-for-vaccinating-immunosuppressed-individuals-with-third-primary-dose.pdf.
2. Australian Government Department of Health. *ATAGI recommendations on the use of a third primary dose of COVID-19 vaccine in individuals who are severely immunocompromised*. 3 November 2021; Available from: https://www.health.gov.au/resources/publications/atagi-recommendations-on-the-use-of-a-third-primary-dose-of-covid-19-vaccine-in-individuals-who-are-severely-immunocompromised.