



NZSG response to:

**Third Primary Dose of the Pfizer/BioNTech Vaccine Policy
Statement and Clinical Guidance
New Zealand COVID-19 Vaccine and Immunisation Programme
Version 2.0**

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Purpose of this response:

The COVID-19 vaccine is safe and effective, including for people taking immune suppressive therapies. NZSG encourages all gastroenterology patients to receive their first and second vaccine dose. NZSG acknowledges and appreciates the Ministry of Health policy to offer a Third Primary Dose of the Pfizer COVID-19 vaccine to people who are immune compromised, in order to increase antibody titres for people who may have lower titres from the first two vaccines. It is important to offer a united approach in the fight against COVID-19, as well as offer specialist knowledge, reassurance and expertise which is the primary purpose of this document.

NZSG represents specialists who provide care for many patients living with Inflammatory Bowel Disease (IBD), Auto Immune Liver Diseases and Orthoptic Liver Transplant (OLT). This document is to provide practical assistance to our members, as well as other professionals who work with us to care for patients receiving immune suppression for gastroenterology conditions.

We note the following from the guideline:

- That the additional third primary COVID-19 vaccination dose should be administered at least 8 weeks after the second dose,
- Special attention needs to be paid to current or planned immune suppressive therapies (ideally, delay the third vaccine for at least 2 weeks after the period of immune suppression, in addition to time 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.

We offer input particularly for 3.3, where the NZSG offers pragmatic information on drug dosing to support the Policy Statement.

A further goal is to share this mahi e kaupapa with individuals and organisations who share the care of patients with Gastroenterology conditions receiving immunosuppressive therapies.

Practical points for the implementation of the Third Primary COVID-19 vaccine dose

Challenges:

- Identification of patients with GI conditions receiving one or more immunosuppressive medications and who meet criteria
- Communication with these patients
- Writing a prescription
- Completing the consent form
- Administration of the third COVID-19 vaccine dose

Solutions:

There will be local solutions to local problems. NZSG is keen to hear of local solutions, and to share these. Current understanding is that Primary Care General Practitioners will receive funding to consent for and provide the Third Primary COVID-19 vaccine dose.

Korero is encouraged and welcomed.

Please direct any korero / feedback regarding this draft guideline to: office@nzsg.org.nz

Third Primary Dose of the COVID-19 vaccine: Inclusion Criteria with NZSG Practice Points

Key:

In black are the MOH Inclusion Criteria relevant to Gastroenterology.

In blue are specific guidance from NZSG for inclusion criteria relevant to gastroenterology.

2. Consumers on immunosuppressive or immunomodulating therapy at the time of vaccination

2.1 Those who were receiving or had received immunosuppressive therapy for a **solid organ transplant** in the previous six months.

Patients: NZSG's interpretation of this guideline is that all patients who have had a solid organ transplant at any time over the age of 12 years meet criteria. All such patients would be on lifelong immunosuppressive medications, and would therefore meet this criterion. These patients are often on multiple medications, such as tacrolimus, mycophenolate mofetil, ciclosporin and/or prednisone

Timing: If treatment for rejection with higher dose immune suppression is needed, then the timing of the third primary dose of COVID-19 vaccine could be 2 weeks after cessation of this treatment as per guidelines, at least 8 weeks after the second vaccine dose. It is not possible to stop routine immune suppression because of the risk of rejection, therefore timing of the third primary dose for people who are stable on treatment can be any time from 8 weeks after the second dose.

2.2 Those who were receiving or had received in the previous three months **targeted therapy for autoimmune disease**, such as JAK inhibitors or biologic immune modulators including B-cell targeted therapies (including rituximab but in this case the recipient would be considered immunosuppressed for a six month period), T-cell co-stimulation modulators, monoclonal tumor necrosis factor inhibitors (TNFi), soluble TNF receptors, interleukin (IL)-6 receptor inhibitors, IL-17 inhibitors, IL 12/23 inhibitors, IL 23 inhibitors. Note: This list is not exhaustive but provides a guide on the types of scenarios where a consumer should receive a third primary dose.

Adalimumab: Anti-TNF

Many people living with IBD receive Adalimumab, a subcutaneous medication. They often receive induction with 160mg at week 0, 80mg week 2, and then continue with 40mg fortnightly. Some people require weekly Adalimumab.

Timing: Patients on Adalimumab should receive their third primary dose of COVID-19 vaccine at least 8 weeks after their second vaccine, and ideally the day before the maintenance Adalimumab is normally given

Infliximab: Anti-TNF

This medication is typically given at a dose of 5mg/kg intravenously to treat IBD. Induction is often prescribed at weeks 0, 2 and 6. Most patients receive an infusion of 5mg/kg every 8 weeks for maintenance therapy: some get a higher dose, or receive infusions closer together.

Timing: Patients receiving Infliximab should receive their third primary dose of COVID-19 vaccine at least 8 weeks after their second vaccine, and ideally 2 – 3 days prior to their next maintenance Infliximab infusion so that the amount of drug is at its lowest

Tofacitinib: JAK3

Some patients may be receiving Tofacitinib as part of a trial, or are self-funding to treat severe ulcerative colitis. This is an oral drug, given at 10mg BD for 8-week induction, then 5mg BD for maintenance.

Timing: Patients on Tofacitinib should be offered a third primary dose of COVID-19 vaccine at least 8 weeks after their second vaccine, and ideally would wait until the maintenance dose has started. A treatment holiday is unlikely, as this treatment in NZ is third line or as part of a trial

Ustekinumab: IL 12/23 inhibitors (Stellara)

This medication for IBD is given as an infusion for the first dose, subcutaneously for the second dose 4 weeks later, and then maintenance subcutaneous doses 12 weekly. Most patients on Ustekinumab will be in a trial or self-funding because of severe disease.

Timing: Ideally, people on Ustekinumab would receive their third primary dose of COVID-19 vaccine 8 weeks after their second dose, before starting Ustekinumab (as would have recently received anti-TNF treatment or similar). Otherwise, the third primary dose of COVID-19 vaccine can be at least 8 weeks after the last one, and ideally given 2-3 days before receiving a maintenance dose (when the amount of medication is at its lowest)

Anti-Integrin: Vedolizumab.

NZSG acknowledges that the MOH recommendation is not exhaustive and this drug should be handled in a similar way to other biological medications. Most patients on Vedolizumab will be in a trial or self-funding because of severe IBD. This medication is given as an

intravenous infusion, with typical doses of 300mg at weeks 0, 2 and 6, then 8 weekly maintenance infusions thereafter.

Timing: Ideally patients on Vedolizumab would receive their third primary dose of COVID-19 vaccine 8 weeks after their second vaccine, before starting Vedolizumab (as would have recently received anti-TNF or similar). Otherwise, the third primary dose of COVID-19 vaccine can be at least 8 weeks after the second dose, and given 2-3 days before receiving a maintenance infusion of Vedolizumab (when the amount of medication is at its lowest).

Other Medications:

Some patients in gastroenterology receive Rituxumab (B cell targeted therapy). It is commonly prescribed as an 8 weekly infusion. Patients on Rituxumab should be offered a third primary dose of COVID-19 vaccine 2-3 days prior to their next Rituxumab dose, or when the Rituxumab course is finished.

3. Consumers with chronic immune-mediated inflammatory disease who were receiving or had received immunosuppressive therapy prior to vaccination

3.1 Those on, or have been on, **high dose corticosteroids (equivalent to ≥ 20 mg prednisolone per day) for more than 10 days in the previous month.**

Prednisone is commonly prescribed in Aotearoa, and is equivalent per mg to Prednisolone.

IBD and AIH: Patients who have received a standard 6- 8 week tapering course of Prednisone in the month prior to the publication of this guideline in October 2021 will be eligible for a third primary dose of COVID-19 vaccine.

3.2 Those on **long-term moderate dose corticosteroids (equivalent to ≥ 10 mg prednisolone per day for more than four weeks) in the previous three months.**

Patients with IBD can receive a tapering course of Prednisone for 6 – 8 weeks, with typical regimens such as:

40mg daily for one week, 30mg daily for one week, 20mg daily for one week, 15 mg daily for one week, 10 mg daily for one week, 5 mg daily for 1 week.

OR: 40mg for one week, reducing by 5mg per week over 8 weeks.

These courses are equivalent to approx. 20 mg daily, therefore all such patients who have received a standard tapering course of steroids in the previous 3 months will be eligible for a third primary dose of COVID-19 vaccine.

3.3 Those with **non-biological oral immune modulating drugs**, such as methotrexate, azathioprine, 6-mercaptopurine, mycophenolate in the previous three months.

Please note: NZSG's recommendations for 3.3 are different to those in the current policy where specific doses are mentioned. NZSG, in the interests of transparency and communication, welcomes any discussion from members as well as similar organisations. NZSG has opted for a pragmatic approach for these Practice Points based on current prescribing practice, pharmacological knowledge and input from immunology.

Methotrexate:

In gastroenterology, the dose of methotrexate can vary up to 25 mg weekly depending on body weight as well as disease activity. It is the opinion of NZSG that all patients who receive oral or subcutaneous methotrexate to treat inflammatory bowel disease or autoimmune liver disease should be offered a third primary dose of the COVID-19 vaccine.

Timing: Ideally, patients on methotrexate should receive their third primary dose of COVID-19 vaccine the day before the usual methotrexate day (Methotrexate is often prescribed on a Monday for example, so ideally would receive the third dose on Sunday, or alternatively receive their third primary dose of COVID-19 vaccine on Monday morning, and delay methotrexate until Tuesday morning)

Thiopurines: Azathioprine, 6-mercaptoprine and tioguanine (thioguanine):

These medications are commonly prescribed for inflammatory bowel disease and autoimmune liver disease. They are also prescribed for liver transplant. Most patients with these conditions receive medication that is adjusted using therapeutic drug monitoring and disease activity to balance risk and benefit, rather than milligrams per kilogram body weight. NZSG's opinion is that all patients who receive azathioprine, mercaptopurine or tioguanine to treat IBD or autoimmune liver disease are offered a third primary dose COVID-19 vaccination.

Timing: The clearance of thiopurine medication is slow. Being mindful of the current environment of limited therapeutic options for people with inflammatory bowel disease, whether to offer a treatment break for at least 8 weeks prior to the third primary dose of COVID-19 vaccine will require a careful assessment of disease activity over the past 12-24 months, then discussion between the patient and their specialist team members. Many patients may not be able to stop the thiopurine for the third vaccine.

Other immune suppressants: Mycophenolate mofetil, Tacrolimus, Ciclosporin, Everolimus

Sometimes these medications are prescribed out of a transplant setting, for example, for IBD or autoimmune liver disease. NZSG's opinion is that patients receiving these medications for this indication should be offered a third primary dose Covid-19 vaccine.

Timing: The third primary vaccine dose should be timed at least 8 weeks after the second vaccine. Generally, patients who need medications such as Tacrolimus and Mycophenolate have significant disease, and are unli

kely to tolerate a drug holiday: This would require careful consideration between the patient and their treating specialist team.

3.4 Those with certain combination therapies at individual doses lower than above, including those on ≥ 7.5 mg prednisolone per day in combination with other immunosuppressants (other than hydroxychloroquine or sulfasalazine) and those receiving methotrexate (any dose) with leflunomide in the previous three months

Practically speaking, this would include IBD or autoimmune liver disease patients who have received a course of steroids and also take an immune modulator.

Patients who only receive mesalazine to treat Ulcerative Colitis (orally or topically) and have not required a course of steroids are expected to have a good response to two primary COVID-19 vaccines. These individuals may be eligible for a 'booster' vaccine at a later date, which is different to the 'third primary dose of COVID-19 vaccine' described here.

4. Consumers who had received high-dose steroids for any reason in the month before vaccination

4.1 Those who had received high-dose steroids (equivalent to >40 mg prednisolone per day for more than a week) for any reason in the month before vaccination.

This criteria will likely include all patients who have received any course of prednisone (such as described above) to treat IBD or autoimmune liver disease. These patients should be offered a third primary dose of COVID-19 vaccine at least 8 weeks after their second dose of vaccine

Note: Consumers who received brief immunosuppression (≤ 40 mg prednisolone per day) for an acute episode (for example, asthma / chronic obstructive pulmonary disease / COVID-19) and individuals on replacement corticosteroids for adrenal

insufficiency are not considered severely immunosuppressed sufficient to have prevented response to the primary vaccination.

NZSG notes there may be a few patients who receive a very short course of prednisone, in which case they are not considered to be severely immunosuppressed.

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