Ministry of Health

COVID-19 Vaccine Third Dose Recommendations

Version 2.0 October 7, 2021

Highlights of changes

- New Table 1- list of immunosuppressant medications eligible for third doses
- Updated to reflect NACI's recommendations on Booster dose in long-term care residents and seniors living in other congregate settings

This guidance provides basic information only. This document is not intended to provide or take the place of medical advice, diagnosis or treatment, or legal advice.

- Please check the Ministry of Health (MOH) COVID-19 website regularly for updates to this document, mental health resources, and other information.

Background

The Ministry of Health is closely monitoring the prevalence of the Delta variant of concern globally and within Ontario given its increased transmissibility and disease severity compared to previous COVID-19 virus strains.

A complete two-dose COVID-19 vaccine series provides strong protection against COVID-19 infection and severe outcomes, including against the Delta variant of concern, in the general population. Achieving high first and second dose coverage remain the focus of the Ontario's COVID-19 vaccination program. However, for some populations, a third dose may be required as two doses may not provide sufficient protection. The Vaccine Clinical Advisory Group, made up of clinical and public health physician experts, provided a recommendation to the Ministry of Health on the select populations which may be considered for third doses based on sub-optimal or waning immune response to vaccines and increased risk of COVID-19 infection, which was included in the MOH COVID-19 Recommendations for Special Populations on August 18th 2021. The National Advisory Committee on Immunization

(NACI) subsequently released guidance on an Additional dose of COVID-19 vaccine in immunocompromised individuals following 1- or 2- dose primary series on September 10th 2021 and on Booster dose in long-term care residents and seniors living in other congregate settings on September 28, 2021.

A risk/benefit analysis for individual patients is at the center of the collaborative clinician/patient decision-making process. Informed consent for additional doses of COVID-19 vaccine should clearly communicate what is known and unknown about the risks and benefits of a third dose. This should include a discussion of the potential for increased risk of myocarditis and pericarditis following receipt of an mRNA COVID-19 vaccine, which is currently reported more commonly after second doses compared to first doses (NACI, 2021). As a precautionary measure, the additional dose of mRNA vaccine should be deferred in individuals who have experienced myocarditis or pericarditis following any preceding dose of an mRNA COVID-19 vaccine until more information is available (NACI, 2021).

The Ministry of Health and NACI are closely following the research on the safety and effectiveness of a third dose. Recommendations will be re-examined on an ongoing basis as new data emerges. Recommendations will be issued as part of Ontario's ongoing COVID-19 vaccination program as further evidence becomes available. Serological testing is not recommended before or after COVID-19 vaccination (NACI, 2021).

For third doses related to out of province vaccination, see the MOH COVID-19 Guidance for Individuals Vaccinated outside of Ontario/Canada.

Recommendations

The individuals outlined below should receive a third dose of an mRNA COVID-19 vaccine (Pfizer-BioNTech or Moderna), and the same vaccine product as their second dose if readily available (i.e. easily available at the time of vaccination without delay or vaccine wastage). See the COVID-19 Vaccination Recommendations for Special Populations Guidance, for additional considerations for third doses in Children, Adolescents and Youth.

Individuals that received AstraZeneca/COVISHIELD COVID-19 vaccine for their first and second dose are recommended to receive an mRNA vaccine for their third dose unless contraindicated. A booster dose of AstraZeneca/COVISHIELD should only be considered when an mRNA vaccine is contraindicated or inaccessible. Informed consent for an additional dose of viral vector vaccine should include discussion about the lack of evidence on the use of an additional dose of viral vector COVID-19 vaccine in immunocompromised populations and the increased risk of Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT), Capillary Leak Syndrome (CLS), and Guillain-Barre syndrome (GBS) following viral vector COVID-19 vaccines (NACI, 2021).

1. Moderately to Severely Immunocompromised

Certain populations are at increased risk of severe outcomes from COVID-19, and have demonstrated a sub-optimal immune response to a complete two-dose COVID-19 vaccine series due to their underlying condition. See NACI's statement for more information.

There is emerging evidence on safety and immunogenicity following a third dose of a COVID-19 vaccine for those that had not seroconverted following their second dose in select immunocompromised populations. Certain moderately and severely immunocompromised populations may benefit from a third dose to complete an extended primary COVID-19 vaccines series.

Recommendations:

At this time third doses of the COVID-19 vaccines will be offered for the following populations eligible for vaccination with the vaccine product authorized for their age group, to complete an extended primary COVID-19 vaccine series.

- Individuals receiving active treatment[1] (e.g., chemotherapy, targeted therapies, immunotherapy) for solid tumour or hematologic malignancies.
- Recipients of solid-organ transplant and taking immunosuppressive therapy

[1] Active treatment includes patients who have completed treatment within 3 months. Active treatment is defined as chemotherapy, targeted therapies, immunotherapy, and excludes individuals receiving therapy that does not suppress the immune system (e.g. solely hormonal therapy or radiation therapy). See Ontario Health/Cancer Care Ontario's Frequently Asked Questions for more information.

- Recipients of chimeric antigen receptor (CAR)-T-cell therapy or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy).
- Individuals with moderate to severe primary immunodeficiency (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome).
- Individuals with stage 3 or advanced untreated HIV infection and those with acquired immunodeficiency syndrome.
- Individuals receiving active treatment with the following categories of immunosuppressive therapies: anti-B cell therapies[2] (monoclonal antibodies targeting CD19, CD20 and CD22), high-dose systemic corticosteroids (refer to the CIG for suggested definition of high dose steroids), alkylating agents, antimetabolites, or tumor-necrosis factor (TNF) inhibitors and other biologic agents that are significantly immunosuppressive (See Table 1).

For individuals with one of the above immune compromising conditions who have not initiated a COVID-19 vaccine series, individuals in the authorized age group should be immunized with a primary series of three doses of an authorized mRNA vaccine (NACI, 2021).

The Ontario recommended interval between the last dose of the initial primary series and the third dose is at least two months (8 weeks). As per NACI, the minimum interval should be 28 days; however, an interval longer than the minimum 28 days between doses is likely to result in a better immune response. Exact timing should be decided with the treating provider in order to optimize the immune response from the vaccine series and minimize delays in management of their underlying condition. Additionally, the interval should consider risk factors for exposure (including local epidemiology and circulation of variants of concern) and risk of severe disease from COVID-19 infection. Some immunocompromised individuals may still be susceptible after the 1 or 2-dose primary series, so their period of susceptibility until receipt of the additional dose will also increase if the interval between doses is increased.

[2] Active treatment for patients receiving B-cell depleting therapy includes patients who have completed treatment within 12 months

For guidance on the timing of vaccination for transplant recipients and those requiring immunosuppressive therapies, for a more fulsome list of conditions leading to primary immunodeficiency, and for further information on immunosuppressive therapies, refer to Immunization of Immunocompromised Persons in the Canadian Immunization Guide (CIG), Part 3 – Vaccination of Specific Populations.

To protect those who are immunocompromised, it also is strongly recommended that all people that come into close contact (e.g. healthcare workers and other support staff, family, friends, caregivers) with these individuals complete a full two-dose vaccine series (i.e. "ring vaccination"). Immunocompromised individuals and those that come into close contact with them should also continue to follow recommended public health measures for prevention and control of SARS-CoV-2 infection and transmission.

Table 1: List of Immunosuppressant Medications for Third Doses

*This list may not be comprehensive; health care providers may identify patients on other medications that are significantly immunosuppressive. Prescriptions/ medication bottles for the below immunosuppressant medications can be presented for third doses as needed. If an individual presents a prescription of a medication that is not listed in Table 1, they should be directed to their health care provider to receive a referral form/letter for a third dose of the COVID-19 vaccine.

Class	Generic Name(s)	Brand Name(s)
Steroids (>20 mg per day of prednisone or equivalent for at least 2 weeks)[3]	• prednisone	
	• dexamethasone	• Decadron
	• methylprednisolone	• DepoMedrol • SoluMedrol • Medrol

[3] As the dosing information may not be included on the patient's prescription, confirmation of the dosage from the individual presenting their prescription is sufficient.

Class	Generic Name(s)	Brand Name(s)
Antimetabolites	• cyclophosphamide	• Procytox
	• leflunomide	• Arava
	• methotrexate	• Trexall • Metoject • Otrexup • Rasuvo • Rheumatrex
	• azathioprine	• Imuran
	• 6- mercaptopurine (6-MP)	• Purinethol
	• mycophenolic acid	• Myfortic
	• mycophenolate mofetil	• Cellcept
Calcineurin inhibitors/mTOR kinase inhibitor	• tacrolimus	• Prograf • Advagraf • Envarsus PA
	• cyclosporine	• Neoral • Gengraf • Sandimmune
	• sirolimus	• Rapamune
JAK (Janus kinase) inhibitors	• baricitinib	• Olumiant
	• tofacitinib	• Xeljanz
	• upadacitinib	• Rinvoq
Anti-TNF (tumor necrosis factor)	• adalimumab	• Humira • Amgevita • Hadlima • Hulio • Hyrimoz • Idacio
	• golimumab	• Simponi
	• certolizumab pegol	• Cimzia
	• etanercept	• Enbrel • Brenzys • Erelzi

Class	Generic Name(s)	Brand Name(s)
Anti-TNF (tumor necrosis factor)	• infliximab	• Remicade • Avsola • Inflectra • Remsima • Renflexis
Anti-Inflammatory	• Sulfasalazine	• Salazopyrin • Azulfidine
	• 5-Aminosalicylic Acid (ASA)/mesalamine	• Pentasa
Anti-CD20	• Rituximab	• Rituxan • Ruxience • Riximyo • Truxima • Riabni
	• ocrelizumab	• Ocrevus
IL-1 RA (interleukin-1 receptor antagonist)	• anakinra	• Kineret
	• canakinumab	• Ilaris
Anti-IL6	• tocilizumab	• Actemra
	• sarilumab	• Kevzara
Anti-IL12/IL23	• ustekinumab	• Stelara
Anti-IL17	• secukinumab	• Cosentyx
	• ixekizumab	• Taltz
Anti-ILI7R	• brodalumab	• Siliq
Anti-BLyS	• belimumab	• Benlysta
Anti-IL23	• guselkumab	• Tremfya
	• risankizumab	• Skyrizi
Selective T-cell costimulation blocker	• abatacept	• Orencia
	• fingolimod	• Gilenya

Class	Generic Name(s)	Brand Name(s)
S1PR (sphingosine 1-phosphate receptor) agonist	• siponimod	• Mayzent
	• ozanimod	• Zeposia
Phosphodiesterase inhibitors	• apremilast	• Otezla

2. Vulnerable Elderly in Congregate Settings

The potential impact of the risk of transmission of the Delta variant of concern in vulnerable elderly populations who live in high risk settings (i.e. congregate living with other vulnerable, high-risk adults) has been assessed, particularly in the context of emerging literature on the reduced immune response and the more rapid waning of antibody responses in this population. These individuals are at increased risk for severe disease because of their age and underlying medical conditions and are at a higher risk of exposure due to their daily interactions with staff and residents in a congregate living environment. Older Ontarians residing in congregate living settings were prioritized for the COVID-19 vaccine when the vaccines were first authorized; therefore, many completed their COVID-19 vaccination series early in the vaccine roll-out, leaving more time for waning should it occur. As well, many received their vaccines using the manufacturers' recommended interval. Evidence to date suggests that, compared to longer intervals, shorter intervals between first and second doses result in lower immune responses and therefore may also result in more rapid waning of protection, including against variants of concern. Vaccines have been effective against COVID-19 in Long Term Care Homes in the 3-4 months after vaccination, but outbreaks are still occurring. In these outbreaks, fully vaccinated residents are being infected, and in some instances leading to severe illness and death. Offering a third dose of COVID-19 vaccine to this population is intended to help increase protection and prevent outbreaks among this vulnerable population.

There are currently no data available on the use of booster doses in LTCH residents or seniors living in other congregate settings. Studies on mRNA booster doses are underway, and early data in older adults shows a safety profile comparable to the

second dose of the primary series, evidence of boosted immune responses and of increased short-term vaccine effectiveness, See NACI's rapid response on booster dose in long-term care residents and seniors in other congregate settings for more information.

Recommendation:

At this time third doses of the COVID-19 vaccines will be offered for the following groups to boost the primary COVID-19 vaccine series:

- Residents of Long-Term Care Homes (LTCH), Retirement Homes (RH), Elder Care Lodges, and elderly living in other congregate settings[4] (e.g. assisted-living facilities, chronic care hospitals, naturally occurring congregate retirement settings/congregate senior's apartment buildings, etc.).

The recommended interval for residents of LTCH, RH and Elder Care Lodges and elderly living in other congregate settings is at least 5 months (20 weeks) after the second dose. This is consistent with the schedule of other vaccines that similarly utilize an additional dose to boost the immune response to a primary series. This recommended interval will be maintained to ensure consistency in the ongoing Ontario vaccination program for this population. Practically, some residents may receive shorter intervals due to operational considerations when boosting entire facilities.

To protect the vulnerable elderly in congregate care settings, it is strongly recommended that all people that come into close contact (e.g.. healthcare workers and other support staff, family, friends, caregivers) with them complete a full two-dose vaccine series (i.e. "ring vaccination") and also continue to follow recommended public health measures for prevention and control of SARS-CoV-2 infection and transmission.

[4] Public Health Units can use their discretion, in collaboration with partner Ministries as needed, to determine eligible congregate settings.