Ontario

Ministry of Health

COVID-19 Vaccine Third Dose and Booster Recommendations

Version 8.0 April 6, 2022

Highlights of changes

- Expanded eligibility for additional booster for individuals 60 years of age and older as well as First Nation, Inuit and Métis individuals, and their non-Indigenous household members, 18 years of age and older starting April 7, 2022 (page 13)
- Information added for the Novavax COVID-19 vaccine throughout
- Information for 3-dose primary series of Moderna (50mcg) for moderately to severely immunocompromised 6-11 year olds (page 6)
- General re-formatting throughout

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, including the COVID-19 Vaccine Administration Guidance.

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Background

In response to the evolving SARS-CoV-2 virus and variants of concern, the Ministry is recommending boosters doses of COVID-19 vaccines to provide increased protection across the population.

Per the Canadian Immunization Guide (CIG), the intent of a booster dose is to restore protection that may have decreased over time to a level that is no longer deemed sufficient in individuals who initially responded adequately to a complete primary vaccine series. Doses of the COVID-19 vaccines after the primary series are described as booster doses. However, over time, the nomenclature of this additional dose could evolve as the optimal number of doses in a primary series is better understood. Evidence is emerging that vaccine effectiveness against infection and COVID-19 disease decreases with time, and the effectiveness of currently authorized COVID-19 vaccines against the Omicron variant is decreased. Therefore, booster doses are recommended for eligible individuals, to obtain stronger protection.

Evidence from clinical trials suggests that booster doses of mRNA vaccines given six months after the primary series elicited a robust immune response. Real world data suggests that a booster dose provides good short-term vaccine effectiveness and has a safety profile similar to the second dose of the vaccine. There is no evidence on the long-term effectiveness of booster doses, so it remains unknown at this time how long this protective benefit might last. Serological testing is not recommended before or after COVID-19 vaccination (CIG, 2022). See the CIG for more information on the evidence, safety and immunogenicity of COVID-19 booster doses.

The evidence on the risk of myocarditis/pericarditis after a booster dose of an mRNA vaccine is limited, but appears to be lower than the already rare risk after the second dose of the primary series but higher than after the first dose (NACI, 2021). Information for subsequent immunization in individuals who experienced myocarditis (with or without pericarditis) within 6 weeks of receiving a previous dose of an mRNA COVID-19 vaccine is available in the COVID-19 Vaccine Chapter of the CIG.

The National Advisory Committee on Immunization (NACI), the Ontario Immunization Advisory Committee (OIAC), the Ministry of Health (MOH), and Public Health Ontario (PHO) are closely following the research on the safety and effectiveness of additional doses. Recommendations will be re-examined on an ongoing basis as

new data emerges and any updates will be issued as part of Ontario's ongoing COVID-19 vaccination program as further evidence becomes available.

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

For information on the timing of third or booster doses following SARS-CoV-2 infection and booster dose post-vaccination observation periods, see the MOH COVID-19 Vaccine Administration guidance.

Recommended COVID-19 Vaccine Products

Individuals are recommended to receive an mRNA vaccine for their primary series and booster dose(s), due to the strong protection offered and well established safety and effectiveness data (CIG, 2022). People who experienced a severe immediate allergic reaction after a dose of an mRNA COVID-19 vaccine can safely receive future doses of the same or another mRNA COVID-19 vaccine after consulting with an allergist/immunologist or another appropriate physician. See the Canadian Immunization Guide for more information.

A booster dose of Novavax Nuvaxovid may be offered to individuals without contraindications who are not able or willing to receive an mRNA vaccine. As part of informed consent, individuals who are not able or willing to receive an mRNA vaccine should be made aware of the longer-term effectiveness and safety data that is available for the mRNA vaccine products as compared to the other authorized COVID-19 vaccines (NACI, 2022).

A booster dose of a viral vector vaccine should only be offered when all other Health Canada authorized COVID-19 vaccines are contraindicated. Informed consent for a viral vector vaccine should include discussion about 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 and the very limited evidence on the use and effectiveness of an additional dose of viral vector COVID-19 vaccine. (NACI, 2021).

3-Dose Primary Series for Moderately to Severely Immunocompromised

Rationale

- A 3-dose primary series is recommended for moderately to severely immunocompromised individuals with the aim of enhancing the immune response and establishing an adequate level of protection for individuals who may develop no or a sub-optimal immune response to a 2-dose primary series. See the COVID-19 chapter in the Canadian Immunization Guide: Immunocompromised persons for more information.
- There is emerging evidence on the safety and immunogenicity following a third dose of a COVID-19 vaccine for those that have not seroconverted following their second dose in select immunocompromised populations. Certain moderately and severely immunocompromised populations may benefit from a third dose to complete a primary COVID-19 vaccines series.

Recommendations

- A 3-dose primary series of mRNA COVID-19 vaccines is recommended for the following populations eligible for vaccination with the vaccine product authorized for their age group (these recommendations also apply to children aged 5-11 who fall within any of the categories below):
    - Individuals receiving dialysis (hemodialysis or peritoneal dialysis)
    - 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
    - Recipients of chimeric antigen receptor (CAR)-T-cell therapy or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression 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.

- Individuals with moderate to severe primary immunodeficiency (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome)
- Individuals with HIV with prior AIDS defining illness **or** prior CD4 count ≤ 200/mm3 **or** prior CD4 fraction ≤ 15% **or** (in children 5-11 years) perinatally acquired HIV infection
- 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 Canadian Immunization Guide 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 moderately to severely immunocompromised children ages 5-11, the pediatric Pfizer-BioNTech (10mcg) vaccine may be given as a 3-dose primary series. Indirect data from adult populations (≥18 years of age) suggests Moderna (100 mcg) may result in higher vaccine effectiveness after a 2-dose primary series compared to Pfizer-BioNTech Comirnaty (30 mcg) and is associated with a higher seroconversion rate among adult immunocompromised patients (NACI, 2022). Given this potential benefit, administration of the Moderna (50 mcg) vaccine as a 3-dose primary series may be considered for some immunocompromised individuals 6 to 11 years of age, as outlined in the product monograph.
- Immunocompromised individuals 12 years of age and older should be offered the full dose of either Moderna (100 mcg) or Pfizer-BioNTech (30 mcg) as a 3-dose primary series. Immunocompromised individuals between the ages of 12-29 are preferentially recommended to receive Pfizer-BioNTech but may receive Moderna (100mcg) based on clinical discretion.
- The safety and efficacy of Novavax have not been established in individuals who are immunocompromised due to disease or treatment. Informed consent for use of the vaccine in this population should include discussion that there is currently limited evidence on the use of Novavax in this population, while there is evidence on the safety profile and effectiveness of mRNA COVID-19 vaccines in these populations based on real world use with large numbers of individuals (CIG, 2022).

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

- The recommended interval between the second dose and the third dose in the primary series is at least **2 months (56 days).**
    - As per NACI, the minimum interval is 28 days; however, an interval longer than the minimum of 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 the individual's 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 SARS-CoV-2 infection. Some immunocompromised individuals may still be susceptible after the 1 or 2-dose in the primary series, so their period of susceptibility until receipt of the additional dose will also increase if the interval between doses is increased.
- Individuals aged 12 and older who received a 3-dose primary series are recommended to receive a fourth (booster) dose after completion of the primary series. See section below on recommended booster dose intervals for more information.
    - Individuals (12 years of age and older) who were receiving active treatment necessitating a 3-dose primary series are eligible for a fourth (booster) dose, even if not currently receiving active treatment.
- For guidance on the timing of vaccine administration for transplant recipients and those requiring immunosuppressive therapies, 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 stay up to date with their COVID-19 vaccines by receiving all recommended doses (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 Significantly Immunosuppressive Medications

*This list may not be comprehensive; health care providers may identify patients on other medications that are significantly immunosuppressive. Prescriptions for the below immunosuppressant medications can be presented for additional 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 and any subsequent dose(s) of a 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. Equivalent steroid dose (prednisone 20 mg = prednisolone 20 mg = methylprednisolone 16 mg = hydrocortisone 80 mg = dexamethasone 3 mg)

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

Class	Generic Name(s)	Brand Name(s)
Anti-TNF (tumor necrosis factor)	• adalimumab	• Humira • Amgevita • Hadlima • Hulio • Hyrimoz • Idacio
	• golimumab	• Simponi
	• certolizumab pegol	• Cimzia
	• etanercept	• Enbrel • Brenzys • Erelzi
	• infliximab	• Remicade • Avsola • Inflectra • Remsima • Renflexis
Anti-Inflammatory	• Sulfasalazine	• Salazopyrin • Azulfidine
	• 5-Aminosalicylic Acid (ASA)/mesalamine	• Pentasa

Class	Generic Name(s)	Brand Name(s)
Anti-CD20	• Rituximab	• Rituxan • Ruxience • Riximyo • Truxima • Riabni
	• ocrelizumab	• Ocrevus
	• ofatumumab	• Kesimpta
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

Class	Generic Name(s)	Brand Name(s)
S1PR (sphingosine 1-phosphate receptor) agonist	• fingolimod	• Gilenya
	• siponimod	• Mayzent
	• ozanimod	• Zeposia
Phosphodiesterase inhibitors	• Apremilast	• Otezla
Anti-integrin	• vedolizumab	• Entyvio

Third (Booster) Dose Recommendations

Third (booster) doses are recommended for the following groups for based on the ongoing risk of infection due to waning immunity, the ongoing risk of severe illness from COVID-19, the societal disruption that results from transmission of infections, and the adverse impacts on health system capacity from the COVID-19 pandemic.

- All individuals in Ontario aged **≥12 years of age** are eligible to receive a booster dose after completion of a primary two-dose COVID-19 vaccine series[4]
- Ontario strongly recommends that a booster dose of an mRNA vaccine should be offered.

Recommended Third (Booster) Dose Intervals

- Individuals in Ontario aged **12-17 years of age** are eligible to receive a third (booster) dose of the Pfizer-BioNTech COVID-19 vaccine **≥6 months (168 days)** after completion of a primary COVID-19 vaccine series.
    - This interval may be associated with a lower risk of myocarditis with or without pericarditis. With informed consent, individuals 12-17 years of age may receive a third (booster) dose at a minimum of 3 months (84 days) after completion of a primary COVID-19 vaccine series.

[4] For individuals that received a dose of Janssen COVID-19 vaccine (a one dose primary series), this booster dose would be their second dose.

- Individuals in Ontario aged **18 years of age and older** are eligible to receive a third (booster) dose of an mRNA vaccine **≥3 months (84 days)** after completion of a primary COVID-19 vaccine series.

NACI has outlined certain populations for which specific products and/or doses may be preferred for a booster dose, as outlined in **Table 2.** See NACI's guidance on booster COVID-19 vaccine doses for additional rationale and considerations.

Fourth (Booster) Doses for Specific Populations

Individuals 60 Years of Age and Older

Individuals 60 years of age and older are at increased risk for severe disease, hospitalization and death from COVID-19. Many of these individuals are several months past their third (booster) dose which may lead to increased vulnerability due to waning immunity. A fourth (booster) dose should be offered to individuals 60 years of age and older who received their third (booster) dose **five months (140 days)** prior. Individuals 60 years of age and older may receive a fourth (booster) dose at a minimum interval of 3 months (84 days) after their third (booster) dose.

First Nation, Inuit and Métis Adults

First Nation, Inuit and Métis individuals, and their non-Indigenous household members, 18 years of age and older may be offered a fourth (booster) dose **≥five months (140 days)** after their third dose at the discretion of their health care provider. The minimum interval for the fourth (booster) dose is 3 months (84 days).

As per NACI, whether or not booster dose vaccine programs are needed in distinct Indigenous communities should be determined by First Nation, Inuit and Métis leadership and their communities, and with the support of public health partners in accordance with the United Nations Declaration on the Rights of Indigenous Peoples.

Moderately to Severely Immunocompromised Individuals

Moderately to severely immunocompromised individuals aged 12 and older who received a 3-dose primary series are recommended to receive a fourth (booster) dose after completion of the 3-dose primary series. The recommended interval is **6**

months (168 days) after the third dose if 12-17 years of age[5] or **≥3 months (84 days)** after the third dose if 18+.

Residents of Long-Term Care Homes, Retirement Homes, Elder Care Lodges and Older Adults Living in other Congregate Settings

Residents of long-term care homes (LTCH) and retirement homes (RH), Elder Care Lodges, and older adults living in other congregate settings are at increased risk for both COVID-19 infection and severe disease, such as hospitalization and death. Many of these individuals are many months past their third (booster) dose and are increasingly susceptible to COVID-19 infection due to waning immunity (OIAC, 2021). A fourth (booster) dose of an mRNA vaccine is recommended for residents of long-term care homes, retirement homes, Elder Care Lodges and older adults living in other congregate settings providing assisted-living and health services* who received their third (booster) dose at least **three months (84 days)** prior.

*This includes settings providing assistance with: bathing, hygiene, ambulation, feeding, dressing, continence care, skin care, dementia care, provision of meals, administration of medications, nursing, or medical services. Other congregate settings may include chronic care hospitals, or older adults living in congregate settings for people with developmental disabilities, or older adults living in congregate settings focussed on mental health and addictions.

NACI has outlined certain populations for which a specific product and/or doses may be preferred for a booster dose, as outlined in **Table 2**. See NACI's guidance on booster COVID-19 vaccine doses for additional rationale and considerations.

[5] This interval may be associated with a lower risk of myocarditis with or without pericarditis. With informed consent, individuals 12-17 years of age may receive a fourth (booster) dose at a minimum of 3 months (84 days) after the third dose.

Table 2: Rationale and Options for Vaccine Type and Dose offered for COVID-19 Vaccine Booster and 3- Dose Primary Series in Certain Populations

Population	Vaccine type (and dose) for booster and third doses which may be preferred	Rationale or additional considerations
• 12 to 29 year olds (including those moderately to severely immunocompromised)	Pfizer-BioNTech (30 mcg) is recommended. For moderately to severely immunocompromised individuals, the vaccine offered is based on clinical discretion. If Moderna is being used, a 100 mcg dose may be considered.	• Lower reported rates of myocarditis/pericarditis following vaccination with Pfizer-BioNTech (30 mcg) compared to Moderna (100 mcg) • There is currently no data on the use of Moderna (50 mcg dose) booster dose in adolescents 12 to 17 years of age.

Population	Vaccine type (and dose) for booster and third doses which may be preferred	Rationale or additional considerations
• ≥70 year olds • Residents of long-term care homes, retirement homes or seniors in other congregate settings • Moderately to severely immunocompromised individuals aged 30 years of age and older (for 3rd dose as part of the primary series and for the booster dose)[6]	Either Moderna (100mcg or 50mcg) or Pfizer-BioNTech (30mcg) may be considered. If Moderna vaccine is being used as the booster product, a 100 mcg dose may be preferred, based on clinical discretion.	• Data suggest that Moderna COVID-19 vaccine may provide a more robust humoral and cellular immune response. • Moderna (100 mcg) induces somewhat higher antibody levels compared to Pfizer-BioNTech (30 mcg). Protection (against severe disease) from a primary series with Moderna (100 mcg) may be more durable than Pfizer (30mcg). These populations may have less robust immune function (elderly) or a diminished immune response to the vaccine (some immunocompromised individuals). It is possible that Moderna (100 mcg) may induce a better immune response than Moderna (50 mcg). • Currently there are no data comparing the immune responses after a booster vaccination with Moderna (100 mcg) and Pfizer-BioNTech (30 mcg) in these populations.

Population	Vaccine type (and dose) for booster and third doses which may be preferred	Rationale or additional considerations
• For all other populations in whom booster doses are recommended that have not been specified above.	Either Moderna (50 mcg) or Pfizer-BioNTech (30 mcg) are suitable products as a booster dose.	Both Pfizer-BioNTech and Moderna are authorized as booster doses by Health Canada. Individuals who are not willing to receive an mRNA vaccine should be made aware of the longer-term effectiveness and safety data that is available for the mRNA vaccine products as compared to the other authorized COVID-19 vaccines vaccine as part of informed consent.[7] A viral vector vaccine should only be considered when all other authorized COVID-19 vaccines are contraindicated.

[6] Moderately or severely immunocompromised adults receiving a fourth (booster) dose after a 3-dose primary series, are eligible to receive a total of four doses.

[7] See NACI's recommendations on Novavax Nuvaxovid for more information.

Appendix A: List of Immunosuppressive Medications in Alphabetical Order

#

5-Aminosalicylic Acid (ASA)/mesalamine
6- mercaptopurine (6-MP)

A

Abatacept
Actemra
adalimumab
Advagraf
Amgevita
anakinra
apremilast
Arava
Avsola
azathioprine
Azulfidine

B

baricitinib
belimumab
Benlysta
Brenzys
Brodalumab

C

canakinumab
Cellcept
certolizumab
Cimzia
Cosentyx
cyclophosphamide
cyclosporine

E

Enbrel
Entyvio
Envarsus
Erelzi
etanercept

F

fingolimod

G

Gengraf
Gilenya
golimumab
guselkumab

H

Hadlima
Hulio
Humira
Hyrimoz

I

Idacio
Ilaris
Imuran
Inflectra
infliximab
ixekizumab

K

Kesimpta
Kevzara
Kineret

L

Leflunomide

M

Mayzent
Methotrexate
Metoject
mycophenolate mofetil
mycophenolic acid
Myfortic

N

Neoral

O

Ocrelizumab
Ocrevus
ofatumumab
Olumiant
Orencia
Otezla
Otrexup
ozanimod

P

Pentasa
Prednisone* (>20mg/day for 14 or more consecutive days)
Procytox
Prograf
Purinethol

R

Rapamune
Rasuvo
Remicade
Remsima
Renflexis
Rheumatrex
Riabni
Rinvoq
Risankizumab
Rituxan
Rituximab
Riximyo
Ruxience

S

Salazopyrin
Sandimmune
Sarilumab
Secukinumab
Siliq
Simponi
Siponimod
sirolimus
Skyrizi
Stelara
sulfasalazine

T

tacrolimus
Taltz
tocilizumab
tofacitinib
Tremfya
Trexall

Truxima

U

upadacitinib
ustekinumab

V

vedolizumab

X

Xeljanz

Z

Zeposia

*or equivalent steroid dose (prednisone 20 mg = prednisolone 20 mg = methylprednisolone 16 mg = hydrocortisone 80 mg = dexamethasone 3 mg)