Clinical Guidance on COVID-19 Vaccines for People with Significant Neuromuscular Conditions Who Require Respiratory Support

This guidance is intended for health-care providers and is based on known evidence as of June 17, 2021.

Background and Context

This guidance is based on a review of the first two vaccines approved by Health Canada for the prevention of COVID-19 disease caused by the SARS-CoV-2 virus: Pfizer-BioNTech (BNT162b2)[1] and Moderna (mRNA-1273)[2], which are mRNA vaccines, and AstraZeneca/COVISHIELD (ChADOx1-S)[3] which is a replication-defective-adenoviral-vector ('viral vector') vaccine.

Currently, anyone aged 12+ (born in 2009 and earlier) in British Columbia is eligible for COVID-19 immunization. At this time, only the Pfizer-BioNTech mRNA vaccine is authorized for youth aged 12 and above,[3] and we are expecting that Health Canada will authorize the Moderna mRNA vaccine for 12-17 year olds in the near future. Studies of the COVID-19 vaccines in younger children are ongoing.

As per the National Advisory Committee on Immunization (NACI), the two mRNA vaccines authorized in Canada (Pfizer-BioNTech and Moderna) can be interchanged for the second dose to complete the series, if the vaccine received for the first dose is not available or is unknown. No data currently exist on the interchangeability of the COVID-19 mRNA vaccines. However, there is no reason to believe that mRNA vaccine series completion with a different authorized mRNA vaccine product will result in any additional safety issues of deficiency in protection. People should not receive an AstraZeneca vaccine for their second dose.

The AstraZeneca/COVISHIELD COVID-19 vaccine program has been stopped in B.C. for first doses, unless there is a contraindication to the mRNA vaccines, or as advised by the Medical Health Officer or an allergist, due to rare (1:100,000) but serious Vaccine-Induced Thrombotic Thrombocytopenia (VITT) blood clotting events and the large supply of other vaccines without this safety concern. The risk of VITT is six times lower for the second dose (1:600,000). People who received the AstraZeneca/COVISHIELD vaccine for their first dose have the option of receiving AstraZeneca/COVISHIELD or an mRNA vaccine for their second dose. Receiving a mixed vaccine series (AstraZeneca/COVISHIELD for first dose and an mRNA vaccine for the second dose) is permitted based on small studies that suggest that this is likely safe and likely as effective and may be even more effective, but not enough is known to

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make firm conclusions and data collection is ongoing. There may also be heightened side effects experienced with a mixed vaccine series. The BCCDC has prepared two information sheets to help navigate that choice:

> **For health care professionals**: www.bccdc.ca/resource-gallery/Documents/Guidelines%20and%20Forms/Guidelines%20and%20Manuals/Immunization/Vaccine%20Info/COVID-19-vaccine-second-dose-considerations-HCP-QandA.pdf
>
> **For patients**: www.bccdc.ca/Health-Info-Site/Documents/COVID-19_vaccine/AstraZeneca_2ndDose.pdf

Another viral vector vaccine, Janssen/Johnson & Johnson (Ad26.COV2.S), has been approved by Health Canada but will not be part of BC's COVID-19 immunization program at this time. As well, another emerging vaccine candidate developed by Novavax may also be approved by Health Canada in the coming months. This vaccine works differently than the approved vaccines in Canada. This guidance will be updated as more information becomes available.

The current interval between doses observed in British Columbia for the general public is 8 weeks. For individuals who have been designated by the Ministry of Health as Clinically Extremely Vulnerable (CEV), as of June 3rd 2021, the dose interval is in line with the manufacturer's recommended dosing interval (21 days for Pfizer-BioNTech, 28 days for Moderna, 8-12 weeks for AstraZeneca/COVISHIELD).

Patients with neuromuscular conditions with significant respiratory muscle weakness are at increased risk of hospitalization and mortality from COVID-19.[5] This includes individuals with significant diseases of the neurologic system including the brain, spinal cord, motor nerves and muscles who, because of their condition require respiratory support in the form of home ventilation or bilevel positive airway pressure in order to function in daily life.[6,7]

This includes individuals requiring respiratory support with the following conditions:

- Motor neuron disease
- Muscular dystrophy
- Peripheral neuropathy including Guillain Barre Syndrome, Charcot-Marie Tooth disease, critical illness neuropathy
- Myopathies including congenital myopathies, myofibrillar myopathies, metabolic myopathies, critical illness myopathy
- Other neuromuscular conditions where breathing muscles are severely impacted due to their conditions
- While people with spinal cord injury are not considered to be at increased risk of getting infected with the COVID-19 virus,[8] those with a spinal cord injury requiring ventilatory support have the same risk factors as other conditions requiring respiratory support mentioned above, thus the clinical judgment is that their risks are similarly high.

Is COVID-19 immunization recommended for patients with neuromuscular conditions who require respiratory support?

COVID-19 immunization is not contraindicated and should be encouraged for patients with neuromuscular conditions requiring respiratory support, including those who have had COVID-19 infection. This recommendation is based on the following factors:

- Patients with neuromuscular conditions who require respiratory support at baseline are at extremely high risk for morbidity and mortality if they are infected with COVID-19; many would not be able to be extubated if intubation was required.
- Weakness of respiratory muscles in individuals with neuromuscular disorders may result in impaired ability to take a deep breath, impaired cough reflex, and ineffective airway clearance of secretions predisposing to atelectasis and lung infection.[6] Acute respiratory failure may rapidly evolve in patients with chronic respiratory failure secondary to neuromuscular weakness. Risks include prolonged invasive ventilation, deterioration of respiratory or skeletal muscle function or death.[5]

While data specific to the safety and efficacy of COVID-19 vaccines for people with neuromuscular disorders is currently limited, the authors of this guidance agree that the benefits of vaccine-induced immunity against COVID-19 for this population outweigh any theoretical risks of immunization.

Is COVID-19 immunization efficacious and safe for patients with neuromuscular conditions who require respiratory support?

Patients with neuromuscular disease requiring respiratory support were not specifically included in the Pfizer-BioNTech or Moderna vaccine trials; therefore, efficacy in this population is unknown. However, there is no reason to believe the vaccine will be less efficacious in patients with neuromuscular disease requiring respiratory support than in the population studied in the clinical trials. Patients with chronic pulmonary disease comprised 7.8% of patients in the Pfizer-BioNTech vaccine trial and patients with hemiplegia and paraplegia comprised 0.1% of patients in the trial.[10] At the time of publication, there are no known serious warnings or precautions associated with the vaccines in patients with neuromuscular disease.[1,2]

Patients with Duchenne's Muscular Dystrophy (DMD) who require respiratory support and who are receiving deflazacort or prednisone will require additional counseling on efficacy and timing of their vaccine with their treatment, as deflazacort and prednisone are immunosuppressing/immunomodulating. There is limited evidence about the efficacy of the Pfizer BioNTech and Moderna vaccines in people who are immunocompromised due to treatment, as immunocompromised patients were not included in the trials. It is unknown if the currently available COVID-19 vaccines are efficacious in those who take immunosuppressants compared to those who are not considered immunosuppressed.

- It is possible that, because of their immunosuppression from treatment, these patients will have a blunted immune response to the vaccine. Because of their increased risk to COVID-19, the vaccine is recommended for patients with neuromuscular conditions who are immunocompromised, but these patients should be informed that they may have a diminished immune response to any of the authorized COVID-19 vaccines..[9,11] As per NACI, safety data in immunocompromised individuals, including those receiving immunosuppressive therapy, were available from observational studies in people who were taking immunosuppressive therapies. The frequency and severity of adverse events following vaccination with an mRNA COVID-19 vaccine were comparable to that of non-immunocompromised individuals in these studies and what was reported in clinical trials. Safety data in these populations following vaccination with a viral vector vaccine is not available.
- Health-care providers caring for DMD patients being treated with deflazacort or prednisone can refer to the clinical guidance for patients with neuromuscular receiving immunosuppressing/immunomodulating therapy.

Are there any specific contraindications or exceptions for patients with neuromuscular conditions who require respiratory support?

Individuals should not receive a COVID-19 vaccine if they have a history of severe allergic reaction to a previous dose of the respective vaccine or any component of the vaccines.[11] For a list of components in the vaccine and packaging, consult the respective COVID-19 mRNA vaccine product monographs found at:

- Pfizer BioNTech: https://covid-vaccine.canada.ca/info/pdf/pfizer-biontech-covid-19-vaccine-pm1-en.pdf
- Moderna: https://covid-vaccine.canada.ca/info/pdf/covid-19-vaccine-moderna-pm-en.pdf
- AstraZeneca: https://covid-vaccine.canada.ca/info/pdf/astrazeneca-covid-19-vaccine-pm-en.pdf and COVISHIELD: https://covid-vaccine.canada.ca/info/pdf/covishield-pm-en.pdf

People with a history of anaphylaxis without known or obvious cause, and those with suspected hypersensitivity or non-anaphylactic allergy to COVID-19 vaccine components, are advised to consult with an allergist prior to immunization. Health-care providers with patients with a history of severe allergic reactions should refer to the product monographs above to review the full ingredient list. Potential allergens that are known to cause type 1 hypersensitivities in the mRNA vaccines include polyethylene glycol (PEG) in the mRNA vaccines and Polysorbate 80 in the viral vector vaccine.

Health Canada continues to monitor any adverse events following immunization through their post-authorization surveillance process.

COVID-19 vaccines can be given concomitantly with, or any time before or after any other live or inactivated vaccine. This is a change from the previous recommendation for a 14-day interval before or after receipt of a COVID-19 vaccine. The original advice against co-administration was based on a cautionary approach, as specific studies of co-administration with other vaccines have not been performed. However, substantial data have now been collected regarding the safety of COVID-19 vaccines currently authorized by Health Canada. Extensive experience with non-COVID-19 vaccines has demonstrated that immunogenicity and adverse event profiles are generally similar when vaccines are administered simultaneously as when they are administered alone. The basis for this change in recommendation is referenced to general administrative guidance for vaccines and guidance from the US Advisory Committee on Immunization Practice (ACIP).

Are there specific recommendations or considerations for safe and/or most effective vaccine administration?

Individuals with muscle disease may not have adequate deltoid muscle mass, in which case the anterolateral thigh can be used to administer the vaccine.[12]

Otherwise, there are no other specific recommendations that pertain to this population unless they have comorbidities requiring special care, such as being treated with immunosuppressive or immunomodulating therapy, in which case health-care providers can refer to clinical guidance for people with autoimmune neuromuscular disorders receiving immunosuppressive/immunomodulating therapy.

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