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 January 20, 2022.

Background and Context

Patients with neuromuscular conditions with significant respiratory muscle weakness are at increased risk of hospitalization and mortality from COVID-19.[1] 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.[2,3]

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,[4] 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.

This guidance is based on a review of the vaccines approved by Health Canada for the prevention of COVID-19 disease caused by the SARS-CoV-2 virus:

- **mRNA vaccines:** tozinameran (COMIRNATY, Pfizer-BioNTech),[5] elasomeran (SPIKEVAX, Moderna)[6]
- **Replication-defective adenoviral vector vaccine:** ChADOx1-S (VAXZEVRIA, AstraZeneca),[7] Ad26.COV2.S (Janssen COVID-19 Vaccine, Janssen)[8]

Currently, anyone in British Columbia who is 5 years and older is eligible for COVID-19 immunization. Health Canada has authorized COMIRNATY (Pfizer-BioNTech) vaccine made for children aged 5 to 11. NACI has released their statement for

this age group[9]. It is anticipated that SPIKEVAX (Moderna) will be approved shortly for children aged 6 to 11. Both of the mRNA vaccines, COMIRNATY (Pfizer-BioNTech) and SPIKEVAX (Moderna), are currently authorized for youth aged 12-17.

People who receive the mRNA vaccine (COMIRNATY [Pfizer-BioNTech] or SPIKEVAX [Moderna]) for their first dose, will usually be offered the same vaccine for their second dose. However, they may be offered the other mRNA vaccine as the vaccines are very similar. 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 or deficiency in protection.[10] It is not recommended to receive VAXZEVRIA (AstraZeneca) vaccine for the second dose.[11] BC has taken the proactive step to expand booster doses for individuals 18 years and older, starting with people at most risk. All booster doses will be mRNA vaccines.[12]

The VAXZEVRIA (AstraZeneca) 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,[10] due to infrequent (1:50,000) but serious Vaccine-Induced Thrombotic Thrombocytopenia (VITT) blood clotting events after the first dose.[13] The risk of VITT is more than six times lower for the second dose (1:600,000). People who had the VAXZEVRIA (AstraZeneca) vaccine for their first dose have the option of receiving VAXZEVRIA (AstraZeneca) for their second dose, or, receiving an mRNA vaccine as their second dose. Receiving a mixed vaccine series (VAXZEVRIA (AstraZeneca) 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 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/Health-Info-Site/Documents/COVID-19_vaccine/Doctor_letter_Recommendations_AZ_COVISHIELD.pdf)
- **For patients**: Why your 2nd dose is important (www.bccdc.ca/Health-Info-Site/Documents/COVID-19_vaccine/AstraZeneca_2ndDose.pdf)

The Janssen COVID-19 Vaccine (Janssen)[8] one-dose viral vector vaccine is now available in limited supply in B.C. However, mRNA vaccines are preferred over viral vector vaccines due to better effectiveness and immunogenicity of mRNA vaccines and the possible adverse effects specifically associated with viral vector vaccines (e.g., Thrombosis and Thrombocytopenia Syndrome [TTS]).

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.

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.[2] 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.[1]

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 COVID-19 vaccine trials; therefore, efficacy in this population is unknown.[5-8] 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.[15]

The Food and Drug Administration (FDA) have issued a for the Janssen COVID-19 vaccine about the increased risk of developing Guillain-Barré syndrome (GBS) in the 42 days after vaccination.[16] The GBS/CIDP Foundation recommends that patients who have developed their disease within 6 weeks of receiving a COVID-19 vaccination, they should make an informed consent after discussing the risks versus benefits with their healthcare professional about receiving a second dose of vaccine that is of a different type, preferably mRNA, as per the NACI guidance.[17]

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.[14,15] 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.[10] BCCDC has a list of the individual components and their purpose in the vaccines (www.bccdc.ca/health-info/diseases-conditions/covid-19/covid-19-vaccine/vaccines-for-covid-19). For a complete list of components in the vaccine, consult the vaccine monographs found at:

- tozinameran (COMIRNATY, Pfizer BioNTech): https://covid-vaccine.canada.ca/info/pdf/pfizer-biontech-covid-19-vaccine-pm1-en.pdf
- elasomeran (SPIKEVAX, Moderna): https://covid-vaccine.canada.ca/info/pdf/covid-19-vaccine-moderna-pm-en.pdf
- ChADOx1-S (VAXZEVRIA, AstraZeneca): https://covid-vaccine.canada.ca/info/pdf/astrazeneca-covid-19-vaccine-pm-en.pdf
- Ad26.COV2.S (Janssen COVID-19 Vaccine, Janssen): https://covid-vaccine.canada.ca/info/pdf/janssen-covid-19-vaccine-pm-en.pdf

For individuals with a history of anaphylactic reaction to a previous dose of an mRNA COVID-19 vaccine, re-vaccination (i.e., administration of a subsequent dose in the series when indicated) may be offered with the same vaccine or the same mRNA platform if a risk assessment deems that the benefits outweigh the potential risks for the individual and if informed consent is provided. Prior to revaccination, consultation with an allergist or another appropriate physician (e.g., Medical Health Officer) is advised. If re-vaccinated, vaccine administration should be done in a controlled setting with expertise and equipment to manage anaphylaxis, with an extended period of observation of at least 30 minutes after re-vaccination.

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.[18]

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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