Clinical Guidance on COVID-19 Vaccines for People with Autoimmune Neuromuscular Disorders Receiving Immunosuppressive/Immunomodulating Therapy

This guidance is intended for health-care providers and is based on known evidence as of March 13, 2021.

Background and Context

- Some patients with significant autoimmune/inflammatory diseases of the neurologic system (including the brain, spinal cord, motor nerves, neuromuscular junction and muscles – referred to broadly as neuromuscular) require treatment with immunotherapies.¹
- These diseases (including multiple sclerosis, neuromyelitis optica, chronic inflammatory demyelinating polyneuropathy, myasthenia gravis, and inflammatory myopathy) result from immune tolerance dysfunction such that the patient’s immune system attacks their own tissues.
- Patients with neuromuscular conditions who require treatment with immunosuppressive medications are at increased risk of hospitalization and mortality from COVID-19.²
- 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)³ and Moderna (mRNA-1273)⁴. Both of these are mRNA vaccines.
- The authors acknowledge that there are two new vaccines more recently approved by Health Canada: AstraZeneca (ChAdOx1-S)⁵ and Janssen/Johnson & Johnson (Ad26.COV2.S)⁶, both of which are replication defective adenoviral vector vaccines. Future vaccine candidates not yet approved include guidance specific to the emerging vaccine candidate by Novavax, which is a recombinant-subunit-adjuvanted protein vaccine. This guidance will be updated in the future as new information and advice on these other vaccines becomes available.
- At this time, only the Pfizer-BioNTech mRNA vaccine is authorized for youth aged 16 and above. In some special circumstances in British Columbia, people with certain underlying health conditions or who take certain medications and treatments are eligible to receive the COVID-19 vaccine starting at age 16. Those individuals are determined by a provincial expert committee as per B.C.’s COVID-19 Immunization Plan.
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For two-dose vaccines, the current interval between doses observed in British Columbia is up to 120 days for all individuals, including for those with underlying conditions or who are immunocompromised due to disease or treatment.

People were generally excluded from the Pfizer-BioNTech and Moderna COVID-19 vaccine trials if they were on immunosuppressive treatment. Therefore, there are uncertainties as to whether COVID-19 vaccine is efficacious and safe in patients with autoimmune neuromuscular disorders on therapy, as well as to the timing of immunization in relation to their treatments.  

Is COVID-19 immunization recommended for patients with neuromuscular disorders receiving immunosuppressive/immunomodulating therapy?

COVID-19 immunization is not contraindicated and should be encouraged for patients with neuromuscular disorders receiving immunosuppressive/immunomodulating therapy who meet the criteria for COVID-19 immunization per B.C.’s COVID-19 Immunization Plan, including those who have had COVID-19 infection. This recommendation is based on the following review:

- The National Advisory Committee on Immunization recommends that immunosuppressed individuals may be offered the vaccine if the benefits of vaccine outweigh the potential risks.  
- Based on the GBS/CIDP Foundation Global Medical Advisory Board’s statement on January 21, 2021: “Neither the Centers for Disease Control and Prevention (CDC) nor the Food and Drug Administration (FDA) recommends against administration of the COVID-19 vaccine in patients with chronic inflammatory demyelinating polyneuropathy or multifocal motor neuropathy … Even though there is no long-term data yet, there is no scientific reason to think that the vaccine will cause problems in those patients with CIDP or MMN.”
- Based on the statement from the National Multiple Sclerosis (MS) Advisory Board/The Canadian Network of Multiple Sclerosis Clinics Statement on February 10, 2021: “Most people with relapsing and progressive forms of MS should be vaccinated. The risks of COVID-19 disease outweigh any potential risks from the vaccine... The vaccines are not likely to trigger an MS relapse or to worsen your chronic MS symptoms. The risk of getting COVID-19 far outweighs any risk of having an MS relapse from the vaccine.”

While data specific to the safety and efficacy of the Pfizer and Moderna COVID-19 vaccines in people who take immunosuppressant or immunomodulating therapies is not currently available, 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.

The risks of COVID-19 infection to neuromuscular patients treated with immunotherapy include the following factors:

- During the COVID-19 pandemic, patients with neuromuscular disorders may be at greater risk of worse outcomes than otherwise healthy people because of an immunocompromised state related to immunotherapy.
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Immunosuppressive therapies can limit immune competence.\textsuperscript{11} This can affect the risk of infections\textsuperscript{12}; some therapies are associated with an increased risk from particular types of pathogens.

- Patients with autoimmune neuromuscular disorders (such as myasthenia gravis) who are infected with SARS-CoV-2 are frequently admitted to hospitals, have disease exacerbations and a higher mortality than the general population with COVID-19.\textsuperscript{13}
- Patients must continue with immunotherapy to avoid increasing symptoms including weakness of respiratory and bulbar muscles; the risk of relapse may result in permanent disability.
- Infections are a well-recognised trigger of symptom exacerbation in autoimmune conditions such as myasthenia gravis and multiple sclerosis.\textsuperscript{14}
- Individual considerations regarding the appropriateness of the vaccine in patients with neuromuscular disease include, but are not limited to:
  - Level of activity of virus in the patient’s local community
  - Individual risk of severe disease or death in patient contracting SARS-CoV-2 due to their neuromuscular condition and independent of their neuromuscular diagnosis (e.g., age and other comorbidities)
  - Whether family, care providers, and close contacts of the patient can receive immunization if they have no contraindication

Is COVID-19 immunization efficacious and safe for patients with neuromuscular disorders receiving immunosuppressive/immunomodulating therapy?

- Individuals with neuromuscular diseases who are treated with immunosuppressant therapy and immunosuppressed people in general were excluded in phase 3 studies of the Pfizer and Moderna vaccines.\textsuperscript{3, 4} Therefore, 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.

- Individuals with neuromuscular diseases who are taking immunosuppressant therapy should be counseled that no data are currently available on the safety and efficacy of mRNA COVID-19 vaccines in this population.\textsuperscript{1} The immune response in these individuals may be blunted and altered immunocompetence may reduce the effects of immunization. There is limited information on the effectiveness of vaccines in individuals who are on immunosuppressive medications.\textsuperscript{7} However, even reduced efficacy may confer benefits against COVID-19 infections.\textsuperscript{1}

- As immune response to COVID-19 immunization is unknown for those taking immunosuppressant or immunomodulating therapy, patients with neuroimmunological disease who receive the COVID-19 vaccine should continue to closely follow public health recommendations including social distancing, regular hand washing and/or disinfection.

- An increased risk of developing autoimmune or inflammatory disorders was not observed in clinical trial participants who received an mRNA COVID-19 immunization compared to placebo. There is no data regarding the risk of exacerbation of autoimmune neuromuscular disorders by the mRNA COVID-19 vaccines.\textsuperscript{1}
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Are there any specific contraindications or exceptions for patients with neuromuscular disorders receiving immunosuppressive/immunomodulating therapy?

### Allergy to vaccine components

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


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).

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

### Guillain Barre Syndrome (GBS)

Individuals with a history of GBS may receive COVID-19 mRNA vaccines unless they have other contraindications to vaccination.

- No instances of GBS were seen during clinical trials of the Pfizer and Moderna mRNA vaccines, and neither the U.S. Centers for Disease Control and Prevention (CDC) nor the Food and Drug Administration (FDA) recommends against the vaccine due to GBS.
- The incidence of GBS in the United Kingdom decreased by 50% during the first wave of COVID-19, likely due to COVID-19 control measures put in place which reduced the incidence of viral infection generally, compared to the same period during the four years prior.
- An analysis of the genetic and protein structure of SARS-CoV-2 showed that it contains no additional immunogenic material known or proven to drive an immune response that would trigger GBS.

### Bell’s palsy

Cases of Bell’s palsy were reported in participants in the mRNA COVID-19 vaccine clinical trials. However, there was not an excess of Bell’s palsy in the COVID-19 vaccine arm and the FDA does not consider these to be above the rate expected in the general population. They have not concluded these cases were caused by immunization. Therefore, the U.S. CDC recommends that individuals who have previously had Bell’s Palsy may receive an mRNA COVID-19 vaccine.
Multiple Sclerosis

Systematic reviews have not shown that vaccines cause or worsen multiple sclerosis. 18

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

Aligned with the Canadian Rheumatology Association’s guidelines, our recommendations are:

1) For patients on the following medications, there is no need to adjust or delay the medication:
   - Hydroxychloroquine,
   - Prednisone less than 20mg/day,
   - IV Ig,
   - Sulfasalazine,
   - Teriflunamide leflunomide,
   - Mycophenolate,
   - Azathioprine,
   - Oral cyclophosphamide,
   - Tacrolimus tocolizumab,
   - Cyclosporin, interferons,
   - Glatiramer acetate,
   - Dimethyl fumerate,
   - Natalizumab.

2) For patients on the following medications, there are two options:
   a) Do not change medication dosing or
   b) Adjust medication dosing to optimize the immune response to the vaccine:
      i. For patients on weekly methotrexate, an option is to skip the methotrexate dose the following week after each vaccine dose.
      ii. For patients on intravenous cyclophosphamide, an option is to take each vaccine dose at least one week prior to the next cyclophosphamide infusion.
      iii. For patients on rituximab or ocrelizumab, the COVID-19 vaccination should ideally be timed four to five months after their last infusion and two to four weeks prior to their next infusion, when possible, in order to optimize vaccine response. However, in patients who require immediate infusion or who are unable to optimize timing of infusion product and vaccine, it is likely more important to have the COVID-19 vaccine earlier than to delay based on timing of B-cell therapy
      iv. For MS patients who are requiring first or repeat dosing of cladribine or alemtuzumab a delay with bridging of Tysabri could be considered until after full vaccine course plus four weeks. If treatment is required because of active disease, then vaccination will need to be delayed by four to six months after treatment.
      v. For patients on prednisone 20mg/d or higher, consider waiting until the prednisone dose is tapered to below 20mg/d to receive both vaccine doses. 15 (Note: for individuals with Duchenne’s Muscular Dystrophy on deflazacort, Parent Project Muscular Dystrophy and Muscular Dystrophy Canada recommend vaccination on current prednisone dose)
References


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Authors

Dr. Kristine Chapman, Division of Neurology, Department of Medicine, University of British Columbia

Mary Nieforth, Operations Director, Vancouver Acute, Vancouver Coastal Health

Dr. Hannah Briemberg, Division of Neurology, Department of Medicine, University of British Columbia

Dr. Virginia Devonshire, Division of Neurology, Department of Medicine, University of British Columbia

Dr. Yahya Agha-Khani, Division of Neurology, Department of Medicine, University of British Columbia

Dr. Andrea Townsend, Division of Physical Medicine and Rehabilitation, Department of Medicine, University of British Columbia

Dr. Jennifer Yao, Division of Physical Medicine and Rehabilitation, Department of Medicine, University of British Columbia

Dr. Kathryn Selby, Division of Neurology, Department of Pediatrics, University of British Columbia

Dr. Jeremy Road, Division of Respiratory Medicine, Department of Medicine, University of British Columbia

Dr. Marie Wright, Division of Respiratory Medicine, Department of Pediatrics, University of British Columbia