Clinical Guidance on COVID-19 Vaccines for Persons with Autoimmune Rheumatic Diseases

This guidance is intended for health-care providers and is based on known evidence as of November 8, 2022.

Background and Context

The majority of adults and children with autoimmune rheumatic diseases (ARD) require immune modulating therapies for disease control. These therapies put people with ARD at higher risk for infections, particularly viral infections. Imunosuppressed persons have a higher risk of poor outcomes with infections. Although there is limited information about outcomes for people with ARD who develop COVID-19, one international study demonstrated that prednisone and an underlying diagnosis of lupus could be associated with worse outcomes and higher mortality.

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), tozinameran and riltozinameran (COMIRNATY Bivalent original & BA.1, Pfizer-BioNTech), tozinameran and famtozinameran (COMIRNATY Bivalent original & BA.4/BA.4, 1Pfizer-BioNTech), elasomeran (SPIKEVAX, Moderna), elasomeran and imelasomeran (SPIKEVAX Bivalent original & BA.1, Moderna)
- **Viral vector vaccine**: ChADOx1-S (VAXZEVRIA, AstraZeneca), Ad26.COV2.S (JCVODEN, Janssen)
- **Recombinant protein vaccine**: COVID-19 Vaccine (recombinant protein, adjuvanted) (NUVAXOVID, Novavax)
- **Plant based virus-like particle (VLP) vaccine**: COVID-19 Vaccine ([VLP], recombinant, adjuvanted) (COVIFENZ, Medicago)

Currently, anyone in British Columbia (B.C.) who is aged 6 months and older is eligible for COVID-19 immunization. The mRNA vaccine SPIKEVAX (Moderna) and COMIRNATY (Pfizer-BioNTech) have been approved for children 6 months to 11 years of age, with young children getting a smaller dose of the same vaccine used for youth and adults. National Advisory Committee on Immunization (NACI) has released their statement for these age groups.

People who receive the mRNA vaccine (COMIRNATY [Pfizer-BioNTech] or SPIKEVAX [Moderna]) for their first dose, will be offered either mRNA vaccine for subsequent doses, with the exception of preferential recommendations based on age and immunosuppression. B.C. has taken the proactive step to expand booster doses for all individuals 5 years
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and older, not just those at high risk. However, it is particularly recommended for individuals 5-17 years of age who are at higher risk of severe illness due to COVID-19 infection. All booster doses will be mRNA vaccines. For those who are not able, or willing, to receive mRNA vaccines, Novavax is available as an alternative for individuals 18 years of age and older.

**Third doses as part of primary vaccine series:**

Recent studies demonstrate that some people who are immunocompromised develop an improved antibody response after a third dose of vaccine. Therefore, people who are moderately to severely immunocompromised in B.C. are eligible to receive a third dose of an mRNA COVID-19 vaccine as part of their primary vaccine series. NACI recommends the SPIKEVAX (Moderna) for children 6 months to 4 years of age. A minimum interval of 28 days between dose 2 and dose 3 is recommended for those eligible for a third dose. As per the B.C. Immunization Manual, SPIKEVAX (Moderna) is preferred for children 6 months to 4 years of age and COMIRNATY (Pfizer-BioNTech) is recommended for those 5-11 years of age. For individuals 12 years of age and older, SPIKEVAX (Moderna) is preferred for the third dose, but if it is unavailable (or if the individual prefers), COMIRNATY (Pfizer-BioNTech) may be provided.

Specifics on current eligibility for a third dose may be reviewed here: [https://www2.gov.bc.ca/gov/content/covid-19/vaccine/register#immunocompromised](https://www2.gov.bc.ca/gov/content/covid-19/vaccine/register#immunocompromised)

**Booster doses:**

As part of the Fall 2022 booster dose program, B.C. is making plans to offer everyone 5 years and older a booster dose. NACI has been clear this approach will provide the best protection in the Fall and Winter when we’re all spending more time inside and respiratory illness is passed around our communities.

SPIKEVAX BIVALENT BA.1 (Moderna) (50 mcg) is the preferred product in B.C. for moderately to severely immunosuppressed individuals 12 years and older. SPIKEVAX original (Moderna) (100 mcg) primary series has been associated with a higher seroconversion rate among immunocompromised adult patients compared to COMIRNATY original (Pfizer-BioNTech) (30 mcg). In a general population of adults, booster vaccination with SPIKEVAX original (Moderna) (50 mcg) was also found to be more effective than COMIRNATY original (Pfizer-BioNTech) (30 mcg) during a period of Delta followed by Omicron variant dominance. However, these studies were conducted prior to the emergence of the Omicron BA.4/BA.5 Variant of Concern (VOC), and their applicability to all Omicron sublineages is uncertain. Health Canada has recently authorized an adapted version of the SPIKEVAX (Moderna) COVID-19 vaccine that targets the Omicron BA.4/BA.5 subvariants.

**Patients who have tested positive for COVID-19:**

Booster doses may be deferred in those who have tested positive for COVID-19 until 3-6 months from symptom onset or, for asymptomatic cases, from the time of the positive test. This suggested interval is based on immunological principles and expert opinion. When considering whether or not to administer vaccine doses following the suggested 3-6-month interval, biological and social risk factors for exposure (e.g., local epidemiology, circulation of VOCs, living settings) and severe disease should also be taken into account. As these intervals are to be used as a guide, clinical discretion is advised.

COVID-19 vaccination may be offered to individuals at any time following recovery from SARS-CoV-2 infection.
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Intervals between doses:

Individuals requesting a shorter interval between doses should be informed that this actually offers less optimal protection, but their request for an earlier dose should be granted, without need for Medical Health Officer approval, provided the minimum interval between doses has been observed.28

The minimum interval between completion of the primary series, or a previous booster dose, and the Fall booster dose is 3 months. This revised minimum interval additionally applies to pregnant people and aligns with NACI’s updated guidance on COVID-19 vaccines for individuals who are pregnant or breastfeeding. The exception to this is JCVODEN (Janssen) for which the minimum interval is 8 weeks between the single dose of JCVODEN (Janssen) and the booster dose.29

Other vaccines:

VAXZEVRIA (AstraZeneca)7

The VAXZEVRIA (AstraZeneca)7 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,17 due to infrequent (1:50,000) but serious Vaccine-Induced Thrombotic Thrombocytopenia (VITT) blood clotting events after the first dose.30 The Government of Canada is not securing additional VAXZEVRIA doses.

JCVODEN (Janssen)8

The JCVODEN8 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]). A viral vector COVID-19 vaccine should only be considered when all other authorized COVID-19 vaccines are contraindicated or have been refused, due to the reduced effectiveness and the possible adverse effects associated with viral vector vaccines (e.g., TTS).

NUVAXOVID (Novavax)9

NUVAXOVID9 is a different class of vaccination, a protein subunit vaccine that will give British Columbians another option to protect themselves against COVID-19 infection. NUVAXOVID may be offered to individuals for whom COVID-19 mRNA vaccines are contraindicated or have been refused.31 This vaccine is available to people aged 18 years and older. It is a two-dose vaccine and a limited number of doses will be available in B.C.32

COVIFENZ (Medicago)10

COVIFENZ10 is a different class of vaccination, a plant-based virus-like particle vaccine that will give British Columbians another option to protect themselves against COVID-19 infection. COVIFENZ is approved for people who are 18 to 64 years of age. It is a two-dose vaccine and a limited number of doses will be available in B.C.10 This product is not yet available in Canada.
Is COVID-19 immunization recommended for people with autoimmune rheumatic diseases?

COVID-19 vaccines should be encouraged for people with autoimmune rheumatic diseases and are not contraindicated, including those who have had a COVID-19 infection.

- Although the majority of patients with ARD who are immunosuppressed were excluded from clinical trials of the COVID-19 vaccines, the Canadian Rheumatology Association, American College of Rheumatology, and British Rheumatology Association have all released position statements strongly supporting the use of COVID-19 immunization in this population.
- Experts agree that the potential benefits and anticipated desirable effects of COVID-19 immunization outweigh the potential harms in persons with ARD.

While data specific to the safety and efficacy of the COVID-19 vaccines in people who take immunosuppressant or immunomodulating therapies is currently limited, there are data to suggest that the currently available COVID-19 vaccines have efficacy. The authors of this guidance agree that the benefits of COVID-19 immunization with these vaccines outweigh any theoretical risks of immunization.

Is the COVID-19 vaccine efficacious and safe in patients with autoimmune rheumatic diseases?

Adults and children with ARD who take immunosuppressant/immunomodulating therapy were excluded in all of the trials for the COVID-19 vaccines currently approved in Canada. 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.

There is one study that suggests that a third dose of COVID-19 vaccine in immunocompromised patients can increase antibody levels. Small studies on third doses of the mRNA COVID-19 vaccines have shown that immunogenicity (immunity measured in the blood) may increase with a third dose. The safety of a third dose is unknown at this time for ARD, but in these small studies reactions were found to be similar to that of prior doses. The impact of additional doses on the worsening of underlying disease or on rare adverse events, including the risk of myocarditis and/or pericarditis, is unknown at this time.
Informed consent should include discussion about the possibility that individuals who are immunosuppressed may have a diminished immune response to any of the authorized COVID-19 vaccines, as well as a discussion about the emerging evidence on the safety of mRNA COVID-19 vaccines in these populations. The recommendations in this clinical guidance are based on these small observational studies, extrapolation of data from other viral infections, immunology of immunizations and from expert opinion.

When infected, people with ARD can exhibit high variability with respect to clinical presentation, organ involvement, disease severity, comorbidities and medications. If a patient has complicated disease or multiple medical conditions and health-care providers have questions, they are encouraged to reach out to the patient’s rheumatologist for specific guidance.

As the majority of patients with ARD are on immune suppressing medications, there may be blunting of the magnitude and duration of vaccine response compared to the general population. Regardless, the benefits of immunization are considered to outweigh the potential risks.

**Are there any specific contraindications or exceptions for people with autoimmune rheumatic diseases?**

Individuals who have had a severe allergic reaction to an ingredient of one type of COVID-19 vaccine are still able to receive future doses of the other type of vaccine. BCCDC has a list of the individual components and their purpose in the vaccines. For a complete list of components in the vaccine, consult the vaccine monographs found at: [www.bccdc.ca/health-info/diseases-conditions/covid-19/covid-19-vaccine/vaccines-for-covid-19](www.bccdc.ca/health-info/diseases-conditions/covid-19/covid-19-vaccine/vaccines-for-covid-19).

People 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-vaccination is going ahead, 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.

Other than allergy, there are no specific contradictions or exceptions for people with ARD apart from the efficacy and safety considerations outlined above.

COVID-19 vaccines can be given concomitantly with, or any time before or after any other indicated vaccine including the seasonal influenza vaccine.
Are there specific recommendations or considerations for safe and/or most effective administration?

Guidance from the Canadian Rheumatology Association\(^ {33}\) is to continue underlying immunosuppression and disease modifying agents without adjustment around COVID-19 immunization with the exception of Rituximab/Ocrelizumab, and high-dose prednisone as indicated below. Clinical advice to adjust Mycophenolate Mofetil around COVID-19 immunization (when the condition is stable) is derived from the American College of Rheumatology guidelines.\(^ {34}\)

For patients on the following medications, there is no need to adjust or delay the medication:

- Adalimumab
- Anakinra
- Anifrolumab
- Azathioprine
- Belimumab
- Canakinumab
- Certolizumab
- Cyclosporin
- Etanercept
- Golimumab
- Gusulkumab
- Hydroxychloroquine
- Infliximab
- Intravenous immunoglobulin (IVIG)
- Ilekizumab
- Leflunomide
- Methotrexate\(^ *\)
- Oral cyclophosphamide
- Prednisone less than 20mg/day (or equivalent)\(^ *\)
- Sarilumab
- Secukinumab
- Sulfasalazine
- Tacrolimus
- Tocilizumab
- Ustekinumab

\(^*\)For patients on weekly methotrexate, hold (stop) the medication for 2 weeks following COVID-19 vaccination.\(^ {43}\)

For patients on rituximab or ocrelizumab, the COVID-19 immunization 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.
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For patients on **mycophenolate mofetil**, if the disease is stable, hold the medication for one week following a COVID-19 dose.35

*For patients on **prednisone** 20mg/day or higher (or equivalent), consider waiting until the prednisone dose is tapered to below 20mg/d to receive both vaccine doses. Pediatric patients on high-dose steroids should consult with their pediatric rheumatologist to decide on the best time to receive the vaccine.44

**NOTE:** The American College of Rheumatology34 differs from the Canadian Rheumatology Association with adjustment recommendations for the medications as follows. The authors of this guidance document are aligned with the Canadian Rheumatology Association’s recommendations, with the exception of mycophenolate mofetil as described above. However, the American College’s recommendations are available [here](https://www.rheumatology.org), and provided below for reference:

- **For patients on weekly methotrexate (MTX),** an option is to skip the MTX dose the following week after each vaccine dose.
- **For patients on tofacitinib, baricitinib, upadacitinib,** an option is to skip the medication for one week following each vaccine dose.
- **For patients on abatacept weekly injections,** an option is to skip the abatacept one week before and one week after the first dose of vaccine. Continue abatacept through the second dose of vaccine. For IV abatacept, consider timing the first dose of vaccine four weeks post-dose and postpone next infusion by one week. No IV Abatacept adjustments are needed for the second vaccine dose.
- **For patients on intravenous cyclophosphamide,** an option is to take each vaccine dose at least one week prior to the next cyclophosphamide infusion.

**References**


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