Clinical Guidance on COVID-19 Vaccines for People with Sickle Cell Disease

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

Background and Context

Sickle Cell Disease (SCD) is an inherited blood cell disorder predominantly affecting persons of African ancestry with an estimated prevalence of 1/500 African Canadians. Patients with SCD often have underlying cardiopulmonary co-morbidities that may predispose them to poor outcomes if they become infected with SARS-CoV-2. The majority of adult sickle cell patients also have functional asplenia which contributes to infection severity and adverse outcomes.

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),\(^1\) tozinameran and riltozinameran (COMIRNATY Bivalent original & BA.1, Pfizer-BioNTech),\(^2\) tozinameran and famtozinameran (COMIRNATY Bivalent original & BA.4/BA.4, 1Pfizer-BioNTech),\(^3\) elasomeran (SPIKEVAX, Moderna),\(^4\) elasomeran and imelasomeran (SPIKEVAX Bivalent original & BA.1, Moderna)\(^5\)

- **Viral vector vaccine**: ChADOx1-S (VAXZEVRIA, AstraZeneca),\(^6\) Ad26.COV2.S (JCVODEN, Janssen)\(^7\)

- **Recombinant protein vaccine**: COVID-19 Vaccine (recombinant protein, adjuvanted) (NUVAXOVID, Novavax)\(^8\)

- **Plant based virus-like particle (VLP) vaccine**: COVID-19 Vaccine ([VLP], recombinant, adjuvanted) (COVIFENZ, Medicago)\(^9\)

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.\(^10\) National Advisory Committee on Immunization (NACI) has released their statement for these age groups.\(^11,12,13\)

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.\(^14,15\) 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.

**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.

**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.

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.
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Other vaccines:

VAXZEVRIA (AstraZeneca)⁶

The VAXZEVRIA (AstraZeneca)⁶ 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,¹⁴ due to infrequent (1:50,000) but serious Vaccine-Induced Thrombotic Thrombocytopenia (VITT) blood clotting events after the first dose.²⁴ The Government of Canada is not securing additional VAXZEVRIA doses.

JCVODEN (Janssen)⁷

The JCVODEN⁷ 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)⁸

NUVAXOVID⁸ 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.²⁵ 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.²⁶

COVIFENZ (Medicago)⁹

COVIFENZ⁹ 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.⁹ This product is not yet available in Canada.

Is COVID-19 immunization recommended for people with sickle cell disease?

COVID-19 vaccines should be encouraged for adults and youth with sickle cell disease and are not contraindicated, including those who have had COVID-19 infection. This recommendation is based on the following review:

- In a UK cohort study, persons with SCD and SARS-CoV-2 infection have increased hazard ratios of hospitalization (4.87 in men and 6.68 in women) and death (4.41 in men and 5.94 in women).²⁷
- In an American registry study of 784 patients with SCD and SARS-CoV-2 infection (average age 22 years), 50.5% were hospitalized, 8.2% admitted to ICU, 3.1% required ventilatory support, and the death rate was 2.4%.²⁸
A retrospective electronic medical record study identified 312 patients with COVID-19 and SCD between January and September 2020. Those with SCD had higher 2.0 times higher risk of hospitalization, 2.4 times higher risk of pneumonia, and 3.4 times higher risk of pain crisis compared to matched individuals without SCD.29

The U.S. Centers for Disease Control (CDC) identifies SCD among the medical conditions at high risk for severe COVID-19 disease.30

Children with SCD may be at higher risk of morbidity with COVID-19 infection including acute vaso-occlusive events and severe acute chest syndrome requiring exchange transfusion.31

The American Society of Hematology recommends that given the high levels of efficacy for vaccines and the low rates of vaccine-related adverse reactions, providers should encourage SCD patients to receive COVID-19 vaccinations as soon as possible.32

There are data to suggest that the currently available COVID-19 vaccines have efficacy.33 While data specific to the safety and efficacy of COMIRNATY (Pfizer-BioNTech), SPIKEVAX (Moderna), and VAXZEVRIA (AstraZeneca) vaccines in people with sickle cell disease is currently limited, trials studying vaccine efficacy in people with sickle cell disease are ongoing.34 The authors of this guidance agree that the benefits of COVID-19 immunization with these vaccines outweigh any theoretical risks of immunization.35

Are COVID-19 vaccines efficacious and safe for people with sickle cell disease?

As sickle cell disease is considered to be a severe underlying medical condition, persons with sickle cell disease were excluded from the Pfizer-BioNTech and Moderna COVID-19 vaccine clinical trials. While data collection is ongoing24, it is currently unknown if COVID-19 vaccines are as efficacious for patients with sickle cell disease as they were found to be for the clinical trial participants.

Due to the functional asplenia of the majority of people with SCD, persons with SCD are immunocompromised.32 As with most vaccines, there is a potential for blunted immune response in individuals who are immunocompromised due to their disease or treatment.35,36 It is therefore possible that persons with SCD may not respond as well to COVID-19 vaccines as the general population and should continue to follow local public health guidelines and adhere to precautionary infection prevention procedures following immunization for as long as SARS-CoV-2 continues to circulate at high rates in the community.

While not specific to COVID-19 vaccines, persons with SCD may be at risk for developing vaso-occlusive pain crises within a few days of immunization with any vaccine and should be counselled to monitor for symptoms and advise their SCD care providers in the event that they develop symptoms.

Currently, there are no serious safety warnings or precautions associated with the COMIRNATY (Pfizer-BioNTech), SPIKEVAX (Moderna), and VAXZEVRIA (AstraZeneca) vaccines in persons with SCD beyond those of the general population. If vaccination with the VAXZEVRIA (AstraZeneca) vaccine is considered, clinicians should be aware of the rare potential for development of venous or arterial thrombosis accompanied by thrombocytopenia 4 to 30 days after vaccination.30
Are there any specific contraindications or exceptions for people with sickle cell disease?

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.

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-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.

Otherwise, there are no contraindications or exceptions to immunization for individuals within the SCD population beyond those for the general population.

COVID-19 vaccines can be given concomitantly with, or any time before or after any other indicated vaccine.

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

SCD patients receiving chronic red blood cell exchange should be vaccinated within 10 days following exchange to minimize the potential for developing vaso-occlusive pain crises. Otherwise, there are no additional timing considerations for the administration of the COVID-19 vaccine in SCD patients.

References

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