Clinical Guidance on COVID-19 Vaccines for People with Cystic Fibrosis

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

Background and Context

The SARS-CoV-2 (i.e. COVID-19) pandemic has been of particular concern for the cystic fibrosis (CF) community. CF is a multisystem condition with comorbidities that are expected to increase vulnerability to COVID-19 infection.

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.COVID-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 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.\(^16,17\) All booster doses will be mRNA vaccines.\(^18\) 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.¹⁹

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.¹⁹ Health Canada has recently authorized an adapted version of the SPIKEVAX (Moderna) COVID-19 vaccine that targets the Omicron BA.4/BA.5 subvariants.²⁰

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.²¹ 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.²²

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.²³

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
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(1:50,000) but serious vaccine-induced thrombotic thrombocytopenia (VITT) blood clotting events after the first dose.\textsuperscript{24} The government of Canada is not securing additional VAXZEVRIA doses.

**JCVDEN (Janssen)**\textsuperscript{7}

The JCVODEN\textsuperscript{7} 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)**\textsuperscript{8}

NUVAXOVID\textsuperscript{8} 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.\textsuperscript{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.\textsuperscript{26}

**COVIFENZ (Medicago)**\textsuperscript{9}

COVIFENZ\textsuperscript{9} 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.\textsuperscript{9} This product is not yet available in Canada.

**Is COVID-19 immunization recommended for people with CF?**

All Health Canada-approved COVID-19 vaccines should be actively encouraged for people with CF who do not have a contraindication, including those who have had COVID-19 infection. This recommendation is based on the following considerations for people with CF:

**Chronic lung disease**

Essentially all people with CF have a type of lung disease that is termed bronchiectasis. The basic defect in CF leads to chronic infection in the lungs by aggressive organisms such as *Pseudomonas aeruginosa*, which are difficult to eradicate despite appropriate antimicrobials and other therapies.

Over time, progressive and irreversible lung damage secondary to acute and chronic infection occurs. This is also associated with periodic acute infection flares termed pulmonary exacerbations, which require additional oral or intravenous (IV) antibiotic therapy. For the average adult with CF, two to three oral and one IV antibiotic course are received per year. In some patients, this will be much more frequent. For pediatrics with CF, lung disease in the early years is not as marked as in adults, and consistent use of appropriate treatment can slow lung disease progression. However, there are still patients who have frequent pulmonary exacerbations and need for oral and/or IV antibiotics.
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This progression of lung disease accounts for the bulk of morbidity and mortality (approximately 50% of adults have a Forced Expiratory Volume in 1 second [FEV₁] <70%). The underlying lung disease complicated by difficult-to-treat infecting organisms is the primary reason for COVID-19 vulnerability.

Other reasons for COVID-19 susceptibility and poor outcomes in people with CF:

- **Diabetes mellitus**: Present in approximately 40% of adults with CF (dysglycemia is present in approximately 65%), and has been shown to be an independent factor for worse outcomes with COVID-19 infection.
- **Nutritional deficiency**: Approximately 85% of people with CF are pancreatic insufficient, with resultant undernutrition in a large proportion of adults with CF.
- **Chronic liver disease**: Affects approximately 30% of people with CF.
- **Post-transplantation**: In Canada, around 1,500 people with CF have received solid organ transplants (predominantly lung) since 2019. People who have received a solid organ transplant take immunosuppressant medications, which are believed to increase risk of serious disease from COVID-19 infection.

There is a growing evidence base available to understand the risk related to COVID-19 infection in people with CF. A recent publication based on data obtained prior to the introduction of COVID-19 vaccines from 22 countries reported on 1452 individuals with CF and confirmed COVID-19 infection. Of those included in the study, 1 in 5 patients required hospitalization, 1 in 30 required intensive care unit (ICU) admission, and 1 in 75 died. Among non-transplanted individuals, worse outcomes were reported for those of older age, non-white race, lower lung function, low body mass index, and concomitant diabetes; this provides direct support for the postulated comorbidities/clinical features listed above. The CF Registry Global Harmonization Group published findings from a global study on the impact of COVID-19 on children with CF. The study included 105 children with CF under the age of 18 from 13 countries; while infection was mild in most cases, a higher number of hospitalizations was noted in individuals with pre-existing advanced lung disease or poor nutrition.

**Impact of respiratory viruses in people with CF extrapolated from other data**

People with CF commonly experience infections with a number of respiratory viruses including influenza, adenovirus, respiratory syncytial virus (RSV), enteroviruses, and rhinoviruses. These infections are a common cause of pulmonary exacerbations (estimated at >50%), which drive symptom morbidity and hospitalizations, accelerate lung function decline, and increase mortality. Viral infections may also be associated with acquisition of *Pseudomonas aeruginosa* pulmonary infection, which is independently associated with the aforementioned negative outcomes.

A previous meta-analysis showed that 50 to 70% of people with CF testing positive for influenza A (H1N1) required hospitalization, as compared to 7 to 20% of the general population. Approximately 40% of patients never recover to their previous baseline lung function after a CF pulmonary exacerbation.

There is every reason to implicate SARS-CoV-2 infection with similar, if not greater, adverse events. Individuals with other chronic lung diseases also are negatively impacted by viral infections, including chronic obstructive pulmonary disease, severe asthma, and bronchiectasis. Although high-quality evidence is not available, influenza immunization is routinely recommended for people with CF worldwide.
Is the COVID-19 vaccine efficacious and safe for people with CF?

As CF is considered to be a severe underlying medical condition, people with CF were excluded from the Pfizer-BioNTech, Moderna, and AstraZeneca COVID-19 vaccine trials. Data is currently limited as to whether COVID-19 vaccines are as efficacious for people with CF as they were found to be for the clinical trial participants. There are data to suggest that the currently available COVID-19 vaccines have efficacy and there is no reason to believe that the antibody response to immunization should be lower in CF compared to the general population.

**CF transmembrane conductance regulator (CFTR)** gene mutations, which are the cause of CF, do not have clinically relevant impacts on the host and innate immunity. There is no evidence of blunted immune response to other immunizations (e.g., influenza), and immunizations are a routine part of CF care. As well, the relatively younger age of people with CF supports a robust immunological response (<5% of patients are >65 years of age).

People with CF are most often not on maintenance/routine medications that would potentially blunt an immune response to immunization (e.g., oral corticosteroids or immunosuppressive therapies). If a patient has received a lung transplant or other solid organ transplant, please refer to the respective clinical guidance for these individuals.

There is no reason to believe that there are specific safety concerns for immunization in people with CF. A study involving 424 people with CF from Italy aged 12 years and older demonstrated that mRNA-based vaccines against SARS-CoV-2 were well-tolerated and safe in the short-term.

Individuals with CF invariably have chronic lung disease, some more severe in nature. Therefore, if there was an anaphylactic reaction, there is the potential for more severe symptoms and complications. This would be similar to other patient populations with advanced lung disease (but perhaps less so in CF, as cardiovascular comorbidities are generally not present). As such, it is recommended that healthcare providers counseling people with CF follow the allergy contraindications and advice provided below closely, particularly for people with CF with most severe lung disease (i.e., FEV₁ <40% predicted).

Are there any specific contraindications or exceptions for people with CF?

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.

People with a history of anaphylactic reaction to a previous dose of an mRNA COVID-19 vaccine, revaccination (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 revaccination 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 revaccination.
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Health Canada continues to monitor any adverse events following immunization through their post-authorization surveillance process.

Otherwise, there are no specific contraindications or exceptions for people with CF from a disease perspective.

COVID-19 vaccines can be given concomitantly with, or any time before or after any other live or inactivated vaccine.34-37

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

Out of abundance of caution, it is recommended that immunization be delayed in the following circumstances:

- If the patient is currently undergoing treatment, including antibiotics for a pulmonary exacerbation of CF;
- If patient is hospitalized for a CF-related complication like a bowel obstruction or acute pancreatitis.

Immunization delays in these circumstances would be decided on an individual basis by the CF clinician.

References

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