Clinical Guidance on COVID- 19 Vaccines for People with Thalassemia

This guidance is intended for health-care providers and is based on available evidence as of June 16, 2021.

Background and Context

Thalassemia is an inherited blood cell disorder. Patients with both transfusion-dependent thalassemia (TDT) and non-transfusion dependent thalassemia (NTDT) may have risk factors associated severe SARS-CoV-2 infection including iron overload, endocrinopathies like diabetes, asplenia due to previous splenectomy, and coagulopathy.[1]

Some people with thalassemia are at a higher risk for severe COVID-19 infections than others. The Thalassemia International Federation has categorized "**highest risk**" and "**high risk**" thalassemia on the basis of age, disease, and comorbidity related factors.[2]

Persons with a diagnosis of thalassemia and any two of the following can be considered as high to highest risk:

- People over 50 years of age
- Transfusion dependent
- Non-transfused with hemoglobin values chronically below 70 g/L for the past two to three years
- People receiving iron chelation therapy
- Splenectomized persons or persons with asplenia
- Those with comorbidities including diabetes, pulmonary hypertension, endocrine, cardiac, or respiratory disease

This guidance is based on a review of three of the 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] which are mRNA vaccines, and AstraZeneca/COVISHIELD (ChADOx1-S)[5] which is a replication-defective-adenoviral-vector ('viral vector') vaccine.

Currently, anyone aged 12+ (born in 2009 and later) in British Columbia is eligible for COVID-19 immunization. At this time, only the Pfizer-BioNTech mRNA vaccine is authorized for youth aged 12 and above,[3] and we are expecting that Health Canada will authorize the Moderna mRNA vaccine for 12-17 year olds in the near future. Studies of the COVID-19 vaccines in younger children are ongoing.

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As per the National Advisory Committee on Immunization (NACI), the two mRNA vaccines authorized in Canada (Pfizer-BioNTech and Moderna) can be interchanged for the second dose to complete the series, if the vaccine received for the first dose is not available or is unknown. 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 of deficiency in protection.

The AstraZeneca/COVISHIELD COVID-19 vaccine program has been stopped in B.C. for first doses, due to rare (1:50,000) but serious Vaccine-Induced Thrombotic Thrombocytopenia (VITT) blood clotting events and the large supply of other vaccines without this safety concern. The risk of VITT is six times lower for the second dose (1:600,000). People who received the AstraZeneca/COVISHIELD vaccine for their first dose have the option of receiving AstraZeneca/COVISHIELD or an mRNA vaccine for their second dose. Receiving a mixed vaccine series (AstraZeneca/COVISHIELD 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.

Due to the nature of their hematologic condition, it is strongly advised that people with thalassemia who received AstraZeneca as their first dose receive an mRNA vaccine for their second dose whenever possible. The BCCDC has prepared two information sheets to help navigate that choice for the general population:

> **For health care professionals**: www.bccdc.ca/resource-gallery/Documents/Guidelines%20and%20Forms/Guidelines%20and%20Manuals/Immunization/Vaccine%20Info/COVID-19-vaccine-second-dose-considerations-HCP-QandA.pdf
>
> **For patients**: www.bccdc.ca/Health-Info-Site/Documents/COVID-19_vaccine/AstraZeneca_2ndDose.pdf

Another viral vector vaccine, Janssen/Johnson & Johnson (Ad26.COV2.S), has been approved by Health Canada but will not be part of BC's COVID-19 immunization program at this time. 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.

The current interval between doses observed in British Columbia for the general public is 8 weeks. For individuals who have been designated by the Ministry of Health as Clinically Extremely Vulnerable (CEV), as of June 3rd 2021, the dose interval is in line with the manufacturer's recommended dosing interval (21 days for Pfizer-BioNTech, 28 days for Moderna, 8-12 weeks for AstraZeneca/COVISHIELD).

Is COVID-19 immunization recommended for people with thalassemia?

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

- A multicentre, retrospective, cross-sectional study from Iran including TDT and NTDT patients described a death rate of 26.6**%** in patients with confirmed COVID infection by PCR and 25% in those with suspected COVID infection.[7]
- A systematic review identified seven publications with a total of 34 beta thalassemia patients (76.5% had TDT) with a death rate of 26.5%.[8]

While data specific to the safety and efficacy of COVID-19 vaccines in people with thalassemia is currently limited, the authors of this guidance agree that the benefits of COVID-19 immunization with these vaccines outweigh any theoretical risks of immunization.

Are COVID-19 vaccines efficacious and safe for people with thalassemia?

As thalassemia is considered to be a severe underlying medical condition, both adults and children with thalassemia were excluded from the COVID-19 vaccine clinical trials. Therefore, it is unknown if COVID-19 vaccines are as efficacious for patients with thalassemia as they were found to be for the clinical trial participants.

Many people with thalassemia have been splenectomised, which compromises immune function. [9] Chronic transfusion and iron overload are also thought to impair a person with thalassemia's immune response. As with most vaccines, there is a potential for blunted immune response in individuals who are immunocompromised due to their disease or treatment.[10,11] It is therefore possible that people with thalassemia may not respond as well to the vaccine as the general population, and should continue to follow local public health guidelines and adhere to precautionary procedures following vaccination for as long as SARS-CoV-2 continues to circulate at high rates in the community.

Currently, there are no serious warnings or precautions associated with the Pfizer-BioNTech and Moderna mRNA COVID-19 vaccines in persons with thalassemia beyond those of the general population. If vaccination with the ChAdOx1 nCov-19 (AstraZeneca/COVISHIELD) 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.

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

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.[9] For a list of components in the vaccine and packaging consult the respective COVID-19 mRNA vaccine product monographs found at:

- Pfizer BioNTech: https://covid-vaccine.canada.ca/info/pdf/pfizer-biontech-covid-19-vaccine-pm1-en.pdf
- Moderna: https://covid-vaccine.canada.ca/info/pdf/covid-19-vaccine-moderna-pm-en.pdf
- AstraZeneca: https://covid-vaccine.canada.ca/info/pdf/astrazeneca-covid-19-vaccine-pm-en.pdf and COVISHIELD: https://covid-vaccine.canada.ca/info/pdf/covishield-pm-en.pdf

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 to review the full ingredient list. Potential allergens that are known to cause type 1 hypersensitivities in the mRNA vaccines include polyethylene glycol (PEG), and Polysorbate 80 in the viral vector vaccine.

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

Thalassemia patients who have received gene therapy should be immunized in accordance with guidelines for patients who have received high-dose chemotherapy and autologous hematopoietic stem cell transplant.

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

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 administration?

There are no specific timing considerations for the administration of the COVID-19 vaccine relative to treatment other than for patients who are receiving gene therapy. These patients should be immunized according to guidelines for autologous stem cell transplant recipients (e.g., two doses at least two weeks pre-treatment and more than three months post-treatment).

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