



Coronavirus COVID-19

BC Centre for Disease Control | BC Ministry of Health



Clinical Guidance on COVID-19 Vaccines for People with Paroxysmal Nocturnal Hemoglobinuria and Atypical Hemolytic Uremic Syndrome

This guidance is intended for healthcare providers. It is based on known evidence as of April 18, 2023.

This document provides guidance for COVID-19 immunization in patients with paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS).

PNH is a rare, acquired disorder of complement mediated red cell hemolysis associated with a very high chance of thrombosis and, sometimes, neutropenia from associated bone marrow failure. Although data is very limited^{1,2} on the impact of COVID-19 on PNH, rare thrombotic complications have been described³ suggesting that there may be additional chance of severe complications from COVID-19 if PNH patients contract the virus. In addition, other viral infections are well recognized triggers for episodes of hemolysis in PNH which can have life-threatening consequences.

aHUS is a rare kidney disease related to microangiopathy. Although no data has been published on the susceptibility to and impact of COVID-19 on people with aHUS, there are numerous reports of aHUS being triggered in genetically susceptible patients by viral infections including influenza.⁴ Also, COVID-19 is more likely to be severe in patients with kidney diseases and renal involvement is a cardinal feature of aHUS. Crises in aHUS patients can be life-threatening with acute kidney injury and both thrombotic and hemorrhagic complications.

Is COVID-19 immunization recommended for people with PNH and aHUS?

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

- PNH and aHUS are both thromboinflammatory disorders and this pathophysiology overlaps with the cytokine storm environment which characterizes severe COVID-19.⁵ This shared pathophysiology does raise concerns that patients with PNH and aHUS will be more at risk of severe COVID-19 regardless of treatment status for PNH and aHUS.
- PNH and aHUS are both treated with drugs targeting the complement cascade, like eculizumab. While eculizumab may not have a direct negative effect on COVID-19,⁶ severe complications of the underlying PNH or aHUS condition in patients receiving eculizumab have been reported when they contracted COVID-19.^{2,7} Also, eculizumab mediated complement blockade leads to an increased risk of some infections and, in particular, *Neisseria* infections, leading to mandatory meningococcal immunization for treated patients.⁸



- Agreement among professional societies recommending that aHUS and PNH patients receive COVID-19 immunizations.⁹⁻¹²

While data specific to the safety and efficacy of the COMIRNATY (Pfizer-BioNTech), SPIKEVAX (Moderna), and VAXZEVRIA (AstraZeneca) vaccines for people with PNH and aHUS is currently limited, there are data to suggest that the currently available COVID-19 vaccines have efficacy.¹³ 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.

Is COVID-19 immunization efficacious and safe for people with PNH and aHUS?

As both PNH and aHUS are considered to be severe underlying medical diseases, they would have been excluded from the COMIRNATY (Pfizer-BioNTech), SPIKEVAX (Moderna) and VAXZEVRIA (AstraZeneca) vaccine clinical trials. Therefore, it is unknown if the currently available COVID-19 vaccines are as efficacious for patients with PNH and aHUS as they were found to be for the trial population.

Vaccine efficacy may theoretically be reduced in patients with PNH who have been treated with anti-thymocyte globulin for aplastic anemia in the six months prior to receiving the vaccine.⁶ It is expected that this consideration may apply to only a very small number of patients in the province, and the patient's hematologist should inform the patient taking this treatment that the vaccine may not provide optimum protection.

Otherwise, there is nothing from a disease perspective pertinent to PNH and aHUS to suggest that the vaccines would be less efficacious or safe for people with PNH and aHUS than they are for the general population. The mRNA vaccines (COMIRNATY (Pfizer-BioNTech), SPIKEVAX (Moderna)) are not live vaccines, and the VAXZEVRIA (AstraZeneca) vaccine is a replication-defective adenovirus vaccine. Thus, they do not pose a risk to PNH and aHUS patients. The benefits of immunization are expected to be similar to that of the general population.

Are there any specific contraindications or exceptions for patients with PNH and aHUS?

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.¹⁴ 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](#).

COVID-19 vaccines can be given concomitantly with, or any time before or after any other indicated vaccine.¹⁵⁻¹⁸

Other than allergy and the safety and efficacy considerations described above, and the medication timing considerations described below, and there are no specific contraindications or exceptions for people with PNH and aHUS.

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

Patients who are on eculizumab should time their vaccination so it occurs as close as possible to their dose (within days before or days after their dose) due to the theoretical possibility that this may reduce their chance of having exacerbation of their disease related to vaccine administration. Typical eculizumab dosing intervals are biweekly.

Some patients with these disorders may be thrombocytopenic or on anticoagulation medication. Guidance developed for the general population who may be on anticoagulants (e.g., prolonged pressure at the site, etc.) can also be applied to those members of this population as they are at increased bleeding risk.

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