Clinical Guidance on COVID-19 Vaccines for People with Metabolically Unstable Inborn Errors of Metabolism

This guidance is intended for health-care providers and is based on available evidence as of April 18, 2023.

This document provides COVID-19 vaccine guidance for adults and children with metabolically unstable inborn errors of metabolism (IEM) including: urea cycle defects, methylmalonic aciduria, propionic acidemia, glutaric aciduria, and maple syrup urine disease. Patients with other rare IEM may also be determined to be metabolically unstable by British Columbia adult and pediatric experts.

Is COVID-19 immunization recommended for people with metabolically unstable inborn errors of metabolism?

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

- IEM may place a patient at increased risk of complications if they develop intercurrent illness including COVID-19. No data have been published addressing the impact of COVID-19 on most of these disorders; however, a single case report documents that COVID-19 can be a trigger for metabolic decompensation as other viral and bacterial infections.
- Infection may lead to severe complications including metabolic stroke and this phenomenon is well-documented in other viruses including influenza.
- Although data are sparse on immune function in these rare conditions, one study did suggest that some patients with IEM are more prone to unusual infections, which suggests a suppressive effect of the condition on global immune function.
- Metabolic decompensation is very rapid and patients can progress from being well to critical state in a matter of hours. The consequences of metabolic decompensation in these disorders are severe and include cerebral edema, coma and death.
- Also, some of the disorders may be associated with chronic kidney disease which puts the patients at higher risk of severe disease and mortality from COVID-19.
- The European Reference Network recommends that patients with IEM should be immunized against COVID-19.

While data specific to the safety and efficacy of COVID-19 vaccines for people with inborn errors of metabolism 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 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 metabolically unstable inborn errors of metabolism?

As IEM are considered to be severe underlying medical diseases, people with these conditions were excluded from the COVID-19 vaccine clinical trials. Therefore, it is unknown if the currently available COVID-19 vaccines are as efficacious for patients with IEM as they were found to be for the clinical trial participants. There is nothing from a disease or treatment perspective pertinent to IEM to suggest that the vaccines would be less efficacious or safe for people with IEM than they are for the general population.

The COMIRNATY (Pfizer-BioNTech), SPIKEVAX (Moderna) vaccines are not live vaccines, and the VAXZEVRIA (AstraZeneca) vaccine is a replication-defective adenovirus vaccine and does not pose a risk of precipitating metabolic decompensation. Given that intercurrent systemic infections are a known precipitant of decompensation in patients with IEM, an event with life threatening consequences, the benefits of immunization are expected to be similar to the general population.

Are there any specific contraindications or exceptions for patients with metabolically unstable inborn errors of metabolism?

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.

Other than allergy, there are no specific contraindications or exceptions for people with IEM. 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?

Patients who are experiencing a disease flare-up on the day of their vaccine appointment should cancel the appointment and re-book when their condition has stabilized. No additional precautions are required for safe or effective administration in this population.

References

11. BC Centre for Disease Control. Communicable Disease Control Manual Chapter 2: Immunization Part 4 Biological Products. NOVAVAX. 8 July 2022. Available at: http://www.bccdc.ca/health-
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Updated: April 18, 2023


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