Nova Scotia Department of Health and Wellness

IMVAMUNE® Vaccine Information for Healthcare Providers

August 6, 2024

The following document provides guidance to healthcare providers on the use of Imvamune® Providers should also consult the following materials for additional information prior to administering Imvamune:

- Nova_Scotia_Vaccine_Immunoglobin_eligibility.pdf (novascotia.ca)
- Vaccine-Eligibility-for-High-Risk-Conditions.pdf (novascotia.ca)
- IMVAMUNE® Smallpox and Monkeypox Vaccine product monograph
- Smallpox and monkeypox vaccine: Canadian Immunization Guide
- NACI recommendations for IMVAMUNE as a routine publicly funded vaccine.

Use of Imvamune® in Nova Scotia

In response to NACI Interim guidance on the use of Imvamune in the context of a routine immunization program released on May 24, 2024, Imvamune is moving from outbreak response to publicly funded for pre-exposure immunization for those meeting high risk eligibility criteria. Post-exposure prophylaxis guidelines are outlined in the Public Health Nova Scotia Communicable Disease Manual, Mpox Chapter. For further questions, please contact local Public Health.

Information about Imvamune

Product and indication, safety, and efficacy

Imvamune® is a live attenuated, non-replicating third generation smallpox vaccine, produced from the Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN) strain of orthopoxvirus. In 2020 it was approved by Health Canada for active immunization against smallpox, mpox, and related orthopoxviral infections in adults 18 years of age and older at high risk of exposure.

Imvamune® differs from previous generations of smallpox vaccines as it is a non-replicating vaccine in humans. The vaccine contains modified orthopoxvirus that has lost its ability to replicate in human cells. While live vaccines are usually contraindicated in immunocompromised and pregnant persons, Imvamune® may be used in these populations as it is considered a non-replicating vaccine.

Available clinical and post-marketing safety surveillance data on Imvamune® demonstrates that the vaccine is well-tolerated.

Contraindications and precautions

According to the product monograph, Imvamune® is **contraindicated** in the following:

- Patients who are hypersensitive to this vaccine or to any ingredient in the formulation or component of the container.
- For a complete listing, see the Dosage Forms, Composition and Packaging section of the Imvamune Product Monograph.
- Individuals who show hypersensitivity reactions after receiving the first dose of the vaccine should not be given the second dose.

Precautions

- As with other vaccines, vaccination with Imvamune® must be postponed in persons with acute febrile conditions if used for non-emergency (pre-event) prophylaxis.
- Imvamune® should not be offered to individuals who are symptomatic, who meet the definition of suspect, probable, or confirmed case of mpox or who have a prior history of infection with mpox.
- The benefit of protection against infection should be discussed with a healthcare provider and weighed against the potential risk of recurrent myocarditis for individuals with a history of myocarditis/pericarditis linked to a previous dose of live replicating 1st or 2nd generation smallpox vaccine and/or Imvamune®; a precautionary approach is warranted at this time until more information is available.

Special populations

Immunosuppressed individuals

Immunocompromised populations may particularly benefit from vaccination as these populations may be at risk for more severe outcomes if infected. There is clinical trial evidence that Imvamune is safe and induces an immune response in individuals who are infected with human immunodeficiency virus (HIV) (CD4 ≥ 100 cells/mcL). Available evidence suggests that people living with chronic diseases (i.e., uncontrolled HIV, immunosuppression) are likely to have reduced vaccine responses and limited duration of protection. Therefore, immunization of individuals with uncontrolled HIV infection at high risk of mpox exposure should be prioritized.

Pregnant and lactating

If at risk for infection, pregnant populations may particularly benefit from vaccination as these populations may be at risk for severe outcomes from disease. There is insufficient data to inform vaccine-associated risks in pregnancy and safety during lactation has not been established, though at this time there is no reason to believe that vaccination would have any adverse impact on the pregnant or lactating individual, or the fetus or child. The risks due to mpox infection should be weighed against the lack of evidence of vaccine safety.

Children under 18 years of age

Evidence is limited in pediatric populations < 18 years of age, and the current indication of Imvamune® is for individuals 18 years of age and older. Off-label use in pediatric populations may be considered pre- or post-exposure, for those meeting the high-risk condition, with their clinician's discretion. Children may be at higher risk of severe outcomes from mpox infection and may benefit from vaccination. The MVA platform used in the Imvamune® vaccine is being studied as part of the development for other vaccines and indirect evidence from those clinical trials has demonstrated that the platform is well tolerated in recipients under the age of 18.

Atopic dermatitis

Clinical trial evidence demonstrates that Imvamune® is safe and induces an immune response in those with atopic dermatitis. See the *Side effects and adverse events* section for additional information on Imvamune® use in persons with atopic dermatitis.

Side effects and adverse events

There currently are no known serious warnings or precautions associated with Imvamune.

Very common side effects (≥1/10) include headache, nausea, myalgia, fatigue, and injection site reactions

including pain, erythema, swelling, induration, and pruritis. Common side effects (≥1/100 to <1/10) include appetite disorder, pain in extremity, arthralgia, increased body temperature and pyrexia, rigor, and chills, as well as injection site reactions including nodule, discolouration, haematoma, and warmth. Uncommon and rare side effects were also reported, with full details in the product monograph.

Both pre-and post-licensure safety data support the safety of Imvamune®. Most were mild to moderate in intensity and resolved without intervention within 7 days post-immunization, and no unexpected adverse effects (AEs) were identified. There were no confirmed cases of cardiac events and/or pericarditis following immunization. The safety profile of Imvamune® was similar for both immunocompetent and immunocompromised individuals. Serious AEs were rarely reported, specifically, there was no signal for increased risk of myocarditis or anaphylaxis following immunization.

In Imvamune® clinical testing, solicited adverse events were more frequent in those with atopic dermatitis and included transient worsening of atopic dermatitis symptoms. However, the Imvamune® vaccine was developed to overcome severe adverse events in those with atopic dermatitis seen with previous generation smallpox vaccines. Available post-marking surveillance data on Imvamune® also suggests that no cases of skin disease were reported in data from the Canadian National Vaccine Safety Network (CANVAS).

Interactions

Concomitant administration of combination anti-retroviral therapy in the majority of HIV-1 infected study population did not reveal an undesirable interaction regarding the safety and efficacy of Imvamune in clinical testing.

If the need for protection is urgent, Imvamune® given as PEP or pre-exposure prophylaxis (PrEP) *should not be delayed* due to recent receipt of an mRNA COVID-19 vaccine. Post-market safety surveillance data on Imvamune® is now available, and shows the vaccine is well tolerated with no signal for increased risk of myocarditis or anaphylaxis following immunization, and no new or unexpectedly safety concerns, therefore NACI is now recommending Imvamune® immunization can be given concurrently (i.e., same day) or at any time before or after other live or non-live vaccines. If concurrent administration with another vaccine is indicated, immunization of each vaccine should be done in a different anatomic site (e.g., different limb) with separate injection equipment. Interaction with concomitant administration of immunoglobulins and other drugs has not been established.

Imvamune® Dosage and Administration

- *Imvamune should be administered subcutaneously.*
- Each single-use vial of Imvamune® contains one 0.5 mL dose. The product does not require dilution and the entire contents of the vial should be drawn up for each dose using a needle long enough to reach the bottom of the vial. The needle should then be changed to a subcutaneous injection needle and the vaccine should be administered immediately.
- Individuals at high risk of mpox should receive two doses of Imvamune® administered at least 28 days (4 weeks) apart.
- Those who have started a primary series with Imvamune®, in whom more than 28 days has passed without receipt of the second dose, should receive the second dose regardless of time

since the first dose.

Imvamune® Safe Vaccine Storage and Handling

Nova Scotia's supply of Imvamune® will be stored within Nova Scotia Health's bio depots according to the product monograph.

Doses of Imvamune® will be transported to the provider at a temperature of 2°C to 8°C and providers must store the product at this temperature until ready to administer the vaccine. Vials must be protected from light and must not be refrozen once thawed. Up to date storage information can be found in the product monograph and on the Public Health Agency of Canada's Imvamune: Storage temperatures, shelf life, shipment and supportive temperature excursion information webpage.

Imvamune® should be thawed at room temperature before use and should be used immediately upon thawing or can be stored at 2°C to 8°C for the period listed in the product monograph. The vial should be swirled gently (**do not shake**) for 30 seconds before drawing up the vaccine to ensure homogeneity of the product. After thawing, the product should appear as a pale milky homogenous suspension. In case of foreign particulate matter, the vaccine must not be used, and a Vaccine Problem Report should be completed with details of the problem and, if still available, the vaccine should be returned to the Bio-Depot. If the vaccine is no longer available, then a Vaccine Problem Report can be emailed directly to publichealthvaccineorders@nshealth.ca.

Obtaining informed consent

As for all vaccines, informed consent must be obtained before administration of Imvamune®. Informed consent discussions for the use of Imvamune should include:

- The rationale for Imvamune® administration.
- The risks of mpox infection and outcomes of disease.
- The potential benefits associated with Imvamune® which include possible prevention or attenuation of mpox infection.
- The potential risks associated with Imvamune® which include any expected side effects.
- How to manage side effects and when to seek medical attention for adverse events.
- The safety or efficacy of Imvamune®, especially for special populations and in use as PEP for mpox.

In addition to the above, providers should inquire if the recipient of Imvamune:

1. Has current symptoms of or has been determined to be a probable or confirmed case of mpox.
    - Persons showing symptoms of mpox or who meet the definition of suspect, probable, or confirmed case of mpox should not receive Imvamune®.
2. Has allergies to any of the components found in Imvamune®.
    - Imvamune® is contraindicated in persons who are hypersensitive to any ingredients of the vaccine.
3. Is pregnant or breastfeeding.
    - See *Special Populations* section above.
4. Has problems with their immune system or is taking any medications that can affect their immune system.

- See *Special Populations* section above.

5. Has any skin conditions such as atopic dermatitis.
    - See *Special Populations* section above.
6. Has recently received specific medications for mpox treatment.
    - It is unclear if antivirals or immunoglobulins could impact protection offered by Imvamune. Preclinical data from previous generation smallpox vaccines showed decreased immune responses when tecovirimat was administered concurrently with earlier generation smallpox vaccines. A person who is currently receiving antiviral treatment for active mpox infection should not receive Imvamune®.

A generic consent form along with an Imvamune® fact sheet for the vaccine recipient can be found through a link at the Nova Scotia Health Infectious Disease and Immunizations webpage in the immunizations section under the mpox tab.

Reporting Adverse Events Following Immunization (AEFIs)

Ongoing pharmacovigilance for Imvamune® is essential.

An AEFI is any untoward medical occurrence which follows immunization, and which does not necessarily have a causal relationship with the use of a vaccine. All adverse events which are not normally expected and that are temporally related to the administration of the vaccine need to be reported to local public health in accordance with It's the Law: Reporting of Adverse Events Following Immunization. Serious adverse events must be reported within one working day and all other events must be reported within five working days. Providers reporting an AEFI to local public health can obtain the AEFI Form and User Guide from the Public Health Agency of Canada.

Process for accessing Imvamune for Nova Scotians meeting the eligibility criteria for Imvamune

Health care providers can access Imvamune® using Nova Scotia Health's current high-risk process for eligible Nova Scotians at high risk of vaccine preventable diseases.

Process for accessing PEP doses

Close contacts of mpox cases will be assessed by local public health to determine if they have sustained a high-risk exposure. If a close contact meets the definition of a high-risk exposure, direction from a Regional Medical Officer of Health (RMOH) is required to administer Imvamune as post-exposure prophylaxis and the close contact will be referred to a health care provider (HCP) for vaccine administration.

If an individual presents to a HCP with a self-identified exposure to a mpox case, the HCP should contact local Public Health. The public health nurse, in conjunction with the RMOH, will determine the need for contact management, including eligibility for PEP, based on an assessment of the details available.

Upon RMOH direction to administer Imvamune®, the public health nurse will coordinate release of the Imvamune product from the Provincial Bio-Depot, and the Provincial Bio-Depot will subsequently arrange and manage all shipping transportation and logistics to the provider.

Additional Resources

Mpox Public Health Case and Contact Management can be accessed here: Mpox Chapter.

Instruction for flipping off cap for IMVAMUNE.

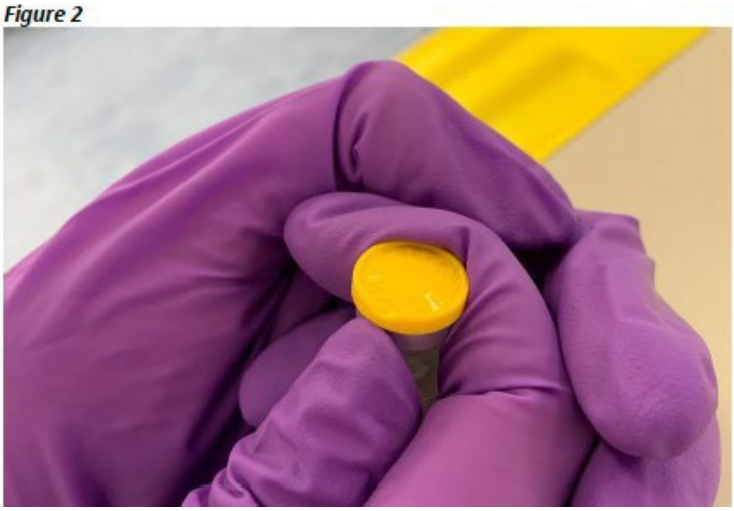
1. On the cap there is a mark for where to flip up the yellow plastic cap, see figure 1a and 1b.

Figure 1a

Figure 1b

2. Hold the vial in your hands and use your thumb to flip up the cap where indicated. See figure 2.

Figure 2



3. Carefully open/flip off the yellow cap to a 90° angel. See figure 3a and 3b.

Figure 3a

Figure 3b

4. Let the cap stay on the metal crimp cap or alternatively flip it all the way off and let the metal crimp cap stay on the stopper/vial to ensure stopper is still fixed to the vial. See figure 4.

Figure 4