Smallpox and Mpox Vaccine

(live-attenuated, non-replicating)

Revision Date: June 30, 2023

Rationale for Update:

- Storage and handling section updated as per product monograph updates from March 10, 2023, and correspondence from the Public Health Agency of Canada.

This policy is evergreen and will be updated as new information becomes available.

Please consult the Product Monograph[1] for further information about the vaccine.	
	IMVAMUNE
Manufacturer	**Bavarian Nordic A/S**
Licensed use	Active immunization against smallpox, mpox and related *orthopoxvirus* infection and disease in adults 18 years of age and older determined to be at high risk of exposure. **Note:** • Imvamune is approved by Health Canada under the provisions of the Extraordinary Use New Drug regulations.
Off-license use	Post-exposure prophylaxis for children from birth up to and including 17 years of age determined to be at high risk of exposure.[10] Pre-exposure use for individuals less than 18 years of age.
Composition/Platform Vaccine Type[1]	• Imvamune is a live, attenuated and non-replicating vaccine produced from the *orthopoxvirus* strain Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN). • Each dose of Imvamune contains 0.5 x 10^8 Inf.U MVA-BN. • MVA-BN has a restricted host-range and fails to replicate in human cells due to multiple genomic deletions and other mutations that block viral assembly and egress in the cells.
Indications for use	**<u>Pre-exposure use in the context of ongoing outbreaks</u>** The following individuals are eligible for pre-exposure Imvamune: • Men who have sex with men (MSM), and individuals who have sex with MSM, and who meet at least one of the following criteria: - Are planning to have, or in the past 90 days have had, two or more sexual partners - Are planning to be, or in the past 90 days have been, in a relationship where at least one of the partners has other sexual partners - Have had a confirmed sexually transmitted infection acquired in the last year - Are planning to engage, or in the past 90 days have engaged, in sexual contact in sex-on-premises venues

	• Individuals who self-identify as sex workers regardless of self- identified sex/gender. • Staff or volunteers in sex-on-premises venues where workers may have contact, or have had contact in the past 90 days, with fomites potentially contaminated with mpox, without the use of personal protective equipment. • Research laboratory employees working directly with replicating orthopoxviruses and who are at high risk of occupational exposure.[10] Notes: ❖ MSM (men who have sex with men) are defined as any male-identifying individual who has sex with another person who identifies as a male, including but not limited to: individuals who self-identify as trans-gender, cis-gender, Two-Spirit, gender-queer, intersex, and non-binary and who also identify as gay, bisexual, or pansexual. ❖ Healthcare workers and clinical diagnostic laboratory workers who are in contact with patients or their clinical diagnostic specimens but who work in environments with training and control measures in place to mitigate risk of unprotected exposures or infections in healthcare settings are not recommended for pre-exposure immunization at this time.[12] **Post-Exposure Prophylaxis** • Contacts with **high exposure risk** with a confirmed case of mpox, or within a setting where transmission is happening. Ideally, within 4 days of the last exposure, and up to a maximum of 14 days after the last exposure. - Contacts with high exposure risk: individuals with direct physical contact (skin/mucosa contact) with a confirmed mpox case while the case is infectious, their body fluids, secretions, skin lesions, contaminated objects or surfaces (e.g. clothing, bedding) without appropriate PPE. - These would include individuals who share a residence, sexual partners, healthcare worker who provided care without appropriate PPE. • Imvamune given within 4 days of exposure may prevent disease. If given 5-14 days following exposure, vaccine may reduce the symptoms of illness, but may not prevent the disease. • Ask about symptoms such as new onset of rash, fever, swollen lymph nodes, fatigue, headache, myalgia, back pain before the immunization. If the contact has developed symptoms since the initial assessment, they should be treated as a probable case and the immunization should not proceed.
Dose	0.5 mL
Route	Subcutaneous injection[1]
Schedule	**Pre-exposure:** ❖ Dose 1: day 0 ❖ Dose 2: 28 days after dose 1[12] • Individuals who receive the second dose beyond the minimum authorized interval (28 days) do not require restarting the series or receiving additional doses. • Individuals considered moderately to severely immunocompromised (see the list below) and currently eligible for pre-exposure immunization are recommended and should be prioritized to receive the second dose at the authorized interval (28 days between doses).

	• Research laboratory employees currently eligible for pre-exposure immunization are recommended to receive the second dose at the authorized interval (28 days between doses). **Post-exposure:** ❖ First dose [10,12] ❖ Second dose*: At least 28 days after first dose[10,12] *** offered to individuals assessed as having ongoing risk of exposure** **Note:** • Individuals who have been diagnosed with mpox infection during this outbreak (beginning in May 2022 in Canada) are not eligible to receive either pre- or post-exposure vaccine at this time because infection likely confers immune protection. • Immunocompetent individuals who have received two doses of Imvamune do not need to receive additional doses after an exposure. However, an additional dose (at least 28 days after the second dose) can be offered to individuals who are moderately to severely immunocompromised (see list below) after an exposure as they may have had a lower or less durable immune response.[11] • Immunocompetent individuals recommended for Imvamune pre-exposure or post-exposure immunization should receive a single dose if they have previously been immunized with a live replicating 1st or 2nd generation smallpox vaccine (i.e., as a booster dose). However, individuals considered moderately to severely immunocompromised should receive two doses, regardless of previous smallpox immunization. • Individuals with the following conditions are considered moderately to severely immunocompromised: - Immunocompromised due to solid tumour or hematologic malignancies or treatments for these conditions - Solid-organ transplant and taking immunosuppressive therapy - Hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy) - Immunocompromised due to chimeric antigen receptor CAR T-cell therapy targeting lymphocytes - Moderate to severe primary immunodeficiency with associated humoral and/or cell-mediated immunodeficiency or immune dysregulation - HIV with AIDS-defining illness or TB diagnosis in the last 12 months before starting vaccine series, or severe immune compromise with CD4<200 cells/u or CD4%<15%, or without HIV viral suppression - Recent treatment with the following categories of immunosuppressive therapies: anti-B cell therapies (monoclonal antibodies targeting CD19, CD20 and CD22), high-dose systemic corticosteroids, alkylating agents, antimetabolites, or tumor necrosis factor (TNF) inhibitors and other biologic agents that are significantly immunosuppressive - Chronic kidney disease on dialysis
Individuals with Immunocompromising Conditions	• Immunocompromised populations may be at risk for more severe outcomes if infected with mpox depending on the nature and degree of the immunosuppression.

	• Live vaccines are usually contraindicated for immunocompromised individuals. However, Imvamune may be used safely in this group as it is considered a non-replicating vaccine.[10] • The use of Imvamune in immunocompromised patients is supported by clinical trials which include individuals who are Human Immunodeficiency Virus (HIV) infected (CD4 ≥ 100 cells/μL) and hematopoietic stem cell transplant (HSCT) recipients (studied two years post HSCT).[1,10] Safety of Imvamune in these populations was comparable to healthy controls. • There were limited data overall on vaccine efficacy, immunogenicity or safety in immunocompromised populations. Compared to people without immunocompromising conditions, immunocompromised populations may have lower immune responses to Imvamune. • Imvamune can be offered to individuals who are immunocompromised due to disease or treatment if informed consent includes discussion about the limited evidence on the use of Imvamune in this population.[10]
Individuals with Atopic Dermatitis[10]	• Imvamune may be safely administered to individuals with atopic dermatitis. • Individuals with atopic dermatitis were a risk group with severe outcomes for earlier generations of smallpox vaccines. • From the limited clinical testing of Imvamune, solicited adverse events were more frequent in this group, including transient worsening of atopic dermatitis. The difference was mostly due to events of mild to moderate severity. • Immune responses were comparable between individuals with and without atopic dermatitis.
Children from birth up to and including 17 years of age	• This population may be at higher risk of severe outcomes from mpox infection and may benefit from immunization.[10] • There is limited safety and efficacy information for use of Imvamune in children.[10] • Indirect evidence of clinical testing of the MVA vector as a viral vector vaccine platform for other vaccines in development (including RSV, TB and Ebola, often at a considerably higher dose than used in Imvamune) indicates that Imvamune components are well tolerated in individuals under 18 years of age.[3,10] • The Bavarian Nordic A/S live-attenuated, non-replicating mpox vaccine (UK product name Imvanex) has been administered safely to children in the United Kingdom for post-exposure prophylaxis, including at least one infant.[3] • Imvamune can be offered to a child either pre-exposure or post-exposure if they meet the eligibility criteria and informed consent includes discussion about the limited evidence on the use of Imvamune in this population.
Pregnancy	• Data available on the use of Imvamune in pregnant people is limited.[1] However, there are no reported safety issues.[9,10] • Animal reproductive studies did not reveal any evidence of impaired fertility or harm to the fetus.[1] • Pregnant individuals may particularly benefit from post-exposure immunization as they may be at risk for severe outcomes from disease.[10] • Live vaccines are usually contraindicated for pregnant individuals. However, Imvamune may be used safely in this group as it is considered a non-replicating vaccine.[10]

	• Imvamune can be offered in pregnancy either pre-exposure or post-exposure if they meet the eligibility criteria and informed consent includes discussion about the limited evidence on the use of Imvamune in this population.
Lactation	• Lactating individuals are not at higher risk for negative outcomes due to mpox infection.[10] • Safety during lactation has not been established as there are no Imvamune studies in this population. It is not known if vaccine components/antigens or antibodies are excreted in human milk; however, this is unlikely as Imvamune is a non-replicating vaccine.[1] At this time, there is no reason to believe that immunization would have any adverse impact on the lactating individual or the child. • Individuals who are breast feeding can be offered Imvamune vaccine either pre-exposure or post-exposure if they meet the eligibility criteria and the lack of evidence on the use of Imvamune in this population has been discussed.[3]
Contraindications[1]	• Known hypersensitivity to any component of Imvamune. - One non-medicinal ingredient in the vaccine that has been associated with allergic reactions in other products is Trometamol (Tris-hydroxymethyl-aminomethane or Tris)[1] a component found in contrast media, oral and parenteral medications. • Anaphylactic reaction to a previous dose of Imvamune.
Other non-medicinal Ingredients	• Contains trace amounts of host (egg) cell DNA and protein, benzonase, gentamicin and ciprofloxacin.[1,10] - Egg-allergic individuals may be immunized using Imvamune, except if there is a known previous anaphylactic reaction to egg. Egg-allergic vaccine recipients should be kept under observation for 30 minutes following the administration of the vaccine. • Sodium chloride • Trometamol • Water for injection • Hydrochloric acid • Bromobutyl rubber stopper • Polypropylene closure **Note:** The *orthopoxvirus* strain used in Imvamune is grown in chicken embryo fibroblast cells.
Precautions	• As with other vaccines, immunization with Imvamune must be postponed in individuals with acute febrile conditions if used for pre-exposure prophylaxis.

Myopericarditis	• Recipients should be advised to seek medical attention if they experience chest pain or discomfort, dyspnea or palpitations.
	  - First and second generation (replicating) smallpox vaccines have been associated with myopericarditis, and although Imvamune is a non-replicating vaccine, there is a theoretical risk of myopericarditis following immunization.[5]
	  - In clinical trials, six cardiac adverse events out of 7,414 subjects (0.08%) were assessed as possibly causally related to the vaccine and presented as: tachycardia, abnormal ECG, palpitations and/or elevated troponins. None of these events were considered serious. Despite close cardiac monitoring, no confirmed case of myocarditis, pericarditis, endocarditis or any other type of cardiac inflammatory disease was recorded.[1]

	• 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, the benefit of pre-exposure or post-exposure immunoprophylaxis to protect against infection versus the risk of recurrent myocarditis/pericarditis should be discussed.[10]
Administration with other products	• Do not delay administration of pre-exposure or post-exposure Imvamune because of recent receipt of COVID-19 mRNA vaccine. - When it is possible, COVID-19 mRNA immunization should be scheduled at least 4 weeks before or after administration of Imvamune. The suggested 4 week interval is precautionary at this time. First generation orthopoxvirus vaccines and mRNA COVID-19 vaccines both have potential risk of cardiac events (myocarditis). Risk of myocarditis/pericarditis with Imvamune is still unknown.[5] • As data on co-administration of Imvamune and other vaccines are not available, it is recommended but not required to wait for a period of at least 14 days between pre-exposure administration of Imvamune and another live or inactivated vaccine if it does not create a barrier to receipt of vaccines.[8] The administration of Imvamune post-exposure should not be delayed for an individuals who has recently received another vaccine.[8] • This vaccine can be administered any time before or after tuberculin skin testing.[8] • Interaction with concomitant administration of immunoglobulins has not been established.[1] • No minimum spacing is required between administration of immunoglobulins or blood products and Imvamune.
Possible reactions[1]	See Product Monograph[1]
Storage and Handling[1]	• When possible, store between -90°C to -70°C. Shelf life when stored at this temperature is 9 years from date of manufacture. After prior long term storage at -90°C to -70°C, vaccine can be stored at -25°C to -15°C for up to 91 days, not exceeding the approved shelf life at -90°C to -70°C[13]. • Shelf life when stored between -60°C to -40°C is 5 years from date of manufacture[13]. • Shelf life when stored between -25°C to -15°C is 3 years from date of manufacture[13]. • Can be stored at +2 to +8°C for up to 2 months[1]. <u>Note:</u> Please contact your local vaccine delivery depot for the date of manufacture. • Transport Imvamune in the frozen (-25 to -15°C) or thawing state. • Refrigerate vaccine that is received in the thawing state at +2 to +8°C. • Thaw vaccine before use. - Thaw time at room temperature is 10 minutes.[13] • After thawing, the product should appear as a milky coloured homogenous suspension. • Swirl gently for 30 seconds. Do not shake. • Do not refreeze. • Protect from light.

Program Notes	2022 June 7 – Implemented in Alberta 2022 July 27 – Updated to include indications for pre-exposure use. 2022 September 21 – Updated to include information about immunity following infection. 2022 October 11 – Updated to expand eligibility for pre-exposure immunization and roll out second doses for pre-exposure immunization. 2022 December 1 – Updated with revised disease name (mpox) from the World Health organization, updated co-administration recommendation and clarification that pre-exposure use in individuals less than 18 years of age is off-license. 2023 March 01 - Updated to expand eligibility for pre-exposure immunization (laboratory research settings). 2023 June 30 - Storage and handling section updated as per product monograph updates from March 10, 2023, and correspondence from the Public Health Agency of Alberta.

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