Ministry of Health

Monkeypox Vaccine (Imvamune®) Guidance for Health Care Providers

Version 2.2 – August 22, 2022

This guidance provides basic information only. This document is not intended to provide or take the place of medical advice, diagnosis or treatment, or legal advice.

Ontario continues to monitor for cases of monkeypox and is working collaboratively with health care providers, Public Health Ontario (PHO) and the Public Health Agency of Canada (PHAC) to address health risk(s). New guidance will continue to emerge as new information becomes available and the epidemiology of this situation evolves.

Imvamune® Vaccine

Imvamune® is a live attenuated, non-replicating vaccine that is approved in Canada for protection against smallpox, monkeypox, and other orthopoxvirus related illness; it is 3rd generation smallpox vaccine. It is produced from the Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN) strain of orthopoxvirus and was developed to provide an alternative for the vaccination of immunocompromised individuals and those with atopic dermatitis, who could not safely receive earlier generation (replicating) smallpox vaccines.

Health Canada first approved the use of this vaccine for active immunization against smallpox in a public health emergency in 2013. In 2020, Health Canada expanded approval of Imvamune® to include additional indications, specifically for monkeypox and related orthopoxvirus infections in adults 18 years of age and older at high risk of exposure. The use of Imvamune® has not been studied in individuals less than 18 years of age or in those who are pregnant or breastfeeding.

Imvamune® can be used as post exposure prophylaxis (PEP) in individuals with a recent high-risk monkeypox exposure. This is based on evidence extrapolated from animal studies and historical experience with smallpox vaccine in humans which suggest that vaccination after an exposure to monkeypox infection may prevent infection or lessen disease severity in those who become infected.

Individuals with signs or symptoms of monkeypox infection should not receive the vaccine as the vaccine is not indicated in the treatment of monkeypox infection.

Use of Imvamune® in Ontario

Given the current supply constraints, Ontario is using a single dose of Imvamune® to limit ongoing transmission. Two doses are recommended for moderately to severely immunocompromised individuals and certain research laboratory employees. This approach is continually being evaluated as the epidemiology and vaccine supply evolve.

Imvamune® should be considered for the following:

1) For the Purposes of Pre-Exposure Prophylaxis (PrEP)

a) Two-spirited, non-binary, trans- or cis-gender individuals who self-identify or have sexual partners who self-identify as belonging to the gay, bisexual and other men who have sex with men (gbMSM) community AND at least one of the following:
   - Have received a diagnosis of bacterial STI (i.e., chlamydia, gonorrhea, syphilis) in the past 2 months;
   - Have had 2 or more sexual partners recently or may be planning to;
   - Have attended venues for sexual contact (i.e., bath houses, sex clubs) recently or may be planning to, or who work/volunteer in these settings; or
   - Have had anonymous sex (e.g., using hookup apps) recently or may be planning to; and/or
   - Are a sexual contact of an individual who engages in sex work.

b) Any individual who engages in sex work or may be planning to.

Household and/or sexual contacts of those identified for PrEP eligibility in parts (a) and (b) above AND are moderately to severely immunocompromised (see Appendix A) or pregnant may be at higher risk for severe illness from a monkeypox infection may be considered for PrEP and should contact their healthcare provider (or their local public health unit) for more information. Also see relevant sections under "Special Populations" for additional considerations.

2) For the Purposes of Post-Exposure Prophylaxis (PEP) throughout Ontario

The provision of Imvamune® for PEP requires an assessment of the risk of exposure by the public health unit. **A single dose** of the vaccine should be offered ideally within 4 days (up to 14 days) from the date of the last exposure to individuals who are a high risk contact of a confirmed or probable case of monkeypox.

Anyone who self-identifies as a high risk contact of a confirmed or probable case of monkeypox should contact their local public health unit for further assessment to see if PEP would be recommended.

Intermediate risk contacts may also be offered PEP, following the public health unit's assessment of individual risks and benefits (i.e., to balance the risks from exposure, protection from vaccination and potential side effects from the vaccine).

PEP is not recommended for low-risk contacts.

Table 1. Recommendations for Post-exposure Prophylaxis (PEP) according to risk of infection

Risk of exposure[1]	**PEP**
High	Recommended
Intermediate	May be recommended based on the public health unit's assessment of risks and benefits
Low	Not recommended
No/very low	Not recommended

1 Monkeypox Virus: Interim Case and Contact Management Guidance for Local Public Health Units

Special Populations

Individuals with History of Previous Smallpox Vaccine

Individuals eligible for Imvamune® as PreP or PEP who previously received either an older generation replicating (live) smallpox vaccine or Imvamune® can be re-vaccinated:

- For individuals with a history of receiving 1 dose of a live smallpox vaccine, a single dose of Imvamune® is recommended.
- For individuals who completed a 2-dose series of Imvamune® more than 2 years ago, a single booster dose of Imvamune® is recommended.
- For individuals who completed a 2-dose series of Imvamune® within the last 2 years, no further doses are recommended.

Individuals Who have had Previous Monkeypox Infection

Individuals who have been a confirmed case of monkeypox in the current outbreak are NOT recommended to receive the monkeypox vaccine at this time; this is based on the limited utility of the vaccine given that these persons are expected to have natural immunity due to recent infection.

Research Laboratory Employees

Research laboratory employees working directly with replicating orthopoxviruses, are eligible to receive two doses of Imvamune® at least 28 days apart as PEP or PrEP if there is an ongoing risk of exposure.

Moderately to Severely Immunocompromised

Individuals who are moderately to severely immunocompromised are eligible to receive two doses of Imvamune® at least 28 days apart. Please refer to:

- Appendix A for the definition of moderate to severe immunocompromise; and
- Appendix B for guidance on how to verify eligibility for second doses in this population.

Clinical trials of Imvamune® have included people living with human immunodeficiency virus (HIV) with a CD4 count of equal or greater than 100. There is less experience in individuals with severe immunosuppression. Additional risk/benefit discussion is indicated for those with severe immunosuppression prior to receiving vaccine as PEP.

Allergy/Hypersensitivity

Individuals who are hypersensitive to this vaccine or to any ingredient in the formulation or component of the container should not receive the vaccine. A list of ingredients can be found in the product monograph.

Note: Imvamune® may contain trace amounts of antibiotics (gentamicin and ciprofloxacin) and egg products (egg cell DNA and protein) which are used during the vaccine production process. Individuals with known hypersensitivity to these products are still able to safely receive Imvamune® but should be monitored for an additional 15 minutes (30 minutes total) after vaccine administration.

Pregnancy and Breastfeeding

There are very limited data on the use of Imvamune® in pregnancy. No clinical trials have been conducted in pregnant individuals, although approximately 300 pregnancies have been reported to the manufacturer with no safety issues identified. There is no data on whether the vaccine is excreted in breastmilk, although this is unlikely as the vaccine is non-replicating. Additional risk/benefit discussion is indicated for those who are pregnant or breastfeeding prior to receiving vaccine as PEP.

Children and Youth

Imvamune® vaccine is not authorized for use in persons under 18 years of age, and has not been studied in this age group, although it has been offered to children as PEP in previous United Kingdom monkeypox incidents as cited in UK PEP guidance. Clinical trials have studied other vaccines (TB and malaria) using Modified Vaccinia Ankara (MVA) as a vector in children with a reassuring safety profile. Additional risk/benefit discussion is indicated for persons under 18 years of age prior to receiving vaccine as PEP.

Persons with Atopic Dermatitis

Persons with atopic dermatitis may have more frequent and more intense reactions after vaccination. This population was specifically studied in clinical trials as those with a history or presence of atopic dermatitis are contraindicated to receive the previous generation of smallpox vaccine (ACAM2000).

Potential Side Effects of Imvamune®

The most common side effects include reactions at the injection site like pain, erythema, induration and swelling. The most common systemic reactions observed after vaccination are fatigue, headache, myalgia, and nausea. Most of the reported adverse drug reactions observed in clinical trials were of mild to moderate intensity and resolved within the first seven days following vaccination.

Older generation (i.e., replicating) smallpox vaccines have been associated with myocarditis. No case of myocarditis or pericarditis was identified in clinical trials of Imvamune®, however post market surveillance of vaccine recipients identified cardiac adverse events of special interest (AESIs) including asymptomatic troponin elevation, abnormal ECG findings, tachycardia, and palpitations. Cardiac AESIs were reported to occur in 1.4% (91/6,640) of Imvamune® recipients and 0.2% (3/1,206) of placebo recipients who were smallpox vaccine-naïve. Individuals should be counselled to seek medical attention if cardiac symptoms (i.e., chest pain, shortness of breath, palpitations) develop following vaccination with Imvamune®.

Informed Consent

The *Health Care Consent Act, 1996* provides specific information as to the consent required for treatment. According to the HCCA, and the College of Nurses of Ontario (CNO) and College of Physicians and Surgeons of Ontario (CPSO) standards, nurses and physicians are accountable for obtaining consent when providing treatment. It is therefore the responsibility of the health practitioner who is proposing the treatment to take reasonable steps to ensure that informed consent for that treatment is obtained.

According to the HCCA, consent to treatment for a capable person is informed if, before giving the consent:

a. the person received the information about the treatment that a reasonable person in the same circumstances would require to make a decision; and
b. the person received responses to his/her requests for additional information about the treatment.

This information must include:

- The nature of the treatment
- The expected benefits of the treatment
- The material risks of the treatment
- The material side effects of the treatment
- Alternative courses of action
- The likely consequences of not having the treatment.

The elements required for consent to treatment include:

- The client must have the capacity to consent
- The consent must relate to the treatment
- The consent must be informed
- The consent must be given voluntarily
- The consent must not be obtained through misrepresentation or fraud.

Evidence of Consent:

Although the HCCA states that consent to treatment may be expressed or implied (i.e., written or verbal), the CNO and CPSO strongly advise nurses and physicians to document that consent was obtained from the client. Examples include: 1) a signed consent form and/or 2) documented consent in the client's health records.

How to order Imvamune®

To order the vaccine, the local public health unit must email the Ministry of Health Emergency Operations Centre at EOCoperations.MOH@ontario.ca or call the Healthcare Provider Hotline at 1-866-212-2272.

Clinicians who think they have a patient (i.e., a contact of a case) who might be recommended to receive PEP using the criteria above should contact their local public health unit.

Co-Administration of Imvamune®

Data on co-administration of Imvamune® and other vaccines are not available. Therefore, it is recommended to not co-administer Imvamune® with other vaccines, and to reschedule any other vaccines until at least 14 days after administration of Imvamune®.

The administration of Imvamune® as post-exposure prophylaxis **should not be delayed** in an individual who has recently received another vaccine.

Storage Conditions

Please see Monkeypox Virus (gov.on.ca) for information on storing Imvamune®.

Reporting Adverse Events Following Immunization

Reports of any Adverse Event Following Immunization (AEFI) following Imvamune® vaccine should be made using the Ontario AEFI form and sent to the local public health unit. Please see Public Health Ontario's vaccine safety webpage and Fact Sheet – Adverse Event Following Immunization Reporting for Health Care Providers in Ontario for additional guidance.

Where can I get more information?

Imvamune® Product Monograph

Ontario Ministry of Health

Public Health Ontario

Public Health Agency of Canada

Additional Resources

Ontario - Monkeypox Virus (gov.on.ca)

World Health Organization – Monkeypox information

World Health Organization - Monkeypox Q&A (who.int)

European Centre for Disease Prevention and Control - Factsheet for health professionals on monkeypox (europa.eu)

United States Centers for Disease Control - Monkeypox | Poxvirus | CDC

Public Health Ontario - Monkeypox Case and Contact Management

Appendix A

Moderately to severely immunocompromised is defined as:

- Individuals receiving dialysis (hemodialysis or peritoneal dialysis)
- Individuals receiving active treatment[1] (e.g., chemotherapy, targeted therapies, immunotherapy) for solid tumour or hematologic malignancies
- Recipients of solid-organ transplant and taking immunosuppressive therapy
- Recipients of chimeric antigen receptor (CAR)-T-cell therapy or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy)
- Individuals with moderate to severe primary immunodeficiency (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome)
- Individuals with HIV with current CD4 count ≤ 200/mm3 **or** prior CD4 fraction ≤ 15% or detectable viral load (i.e., not suppressed)
- Individuals receiving active treatment with the following categories of immunosuppressive therapies: anti-B cell therapies[2] (monoclonal antibodies targeting CD19, CD20 and CD22), high-dose systemic corticosteroids (refer to the Canadian Immunization Guide for suggested definition of high dose steroids), alkylating agents, antimetabolites, or tumor-necrosis factor (TNF) inhibitors and other biologic agents that are significantly immunosuppressive (See Table 2).

[1] Active treatment includes patients who have completed treatment within 3 months. Active treatment is defined as chemotherapy, targeted therapies, immunotherapy, and excludes individuals receiving therapy that does not suppress the immune system (e.g., solely hormonal therapy or radiation therapy). See Ontario Health/Cancer Care Ontario's Frequently Asked Questions for more information.

[2] Active treatment for patients receiving B-cell depleting therapy includes patients who have completed treatment within 12 months.

- For guidance on the timing of vaccine administration for transplant recipients and those requiring immunosuppressive therapies, a more comprehensive list of conditions leading to primary immunodeficiency, and for further information on immunosuppressive therapies, refer to Immunization of Immunocompromised Persons in the Canadian Immunization Guide (CIG), Part 3 – Vaccination of Specific Populations.

Table 2 List of Significantly Immunosuppressive Medications

Individuals can demonstrate their eligibility to receive the second dose of the Imvamune® vaccine by bringing their medications and/or their prescription receipt from the pharmacy to the vaccine clinic.

The table below lists many of the common immunosuppressive medications used in Ontario but it is not an exhaustive list. If an individual is receiving an immunosuppressive biologic agent and they do not have a prescription, or their medication is not listed below, they can receive a referral form/letter indicating their eligibility due to their immunocompromised status from their health care provider to receive a second dose of the Imvamune® vaccine.

Vaccine providers can refer to Appendix B for guidance on how to verify eligibility for second doses at vaccination clinics.

Class	Generic Name(s)	Brand Name(s)
Steroids (>20 mg per day of prednisone or equivalent for at least 2 weeks)	• prednisone	
	• dexamethasone	• Decadron
	• methylprednisolone	• DepoMedrol • SoluMedrol • Medrol

Class	Generic Name(s)	Brand Name(s)
Antimetabolites	• cyclophosphamide	• Procytox
	• leflunomide	• Arava
	• methotrexate	• Trexall • Metoject • Otrexup • Rasuvo • Rheumatrex
	• azathioprine	• Imuran
	• 6- mercaptopurine (6-MP)	• Purinethol
	• mycophenolic acid	• Myfortic
	• mycophenolate mofetil	• Cellcept
Calcineurin inhibitors/mTOR kinase inhibitor	• tacrolimus	• Prograf • Advagraf • Envarsus PA
	• cyclosporine	• Neoral • Gengraf • Sandimmune
	• sirolimus	• Rapamune
JAK (Janus kinase) inhibitors	• baricitinib	• Olumiant
	• tofacitinib	• Xeljanz
	• upadacitinib	• Rinvoq

Class	Generic Name(s)	Brand Name(s)
Anti-TNF (tumor necrosis factor)	• adalimumab	• Humira • Amgevita • Hadlima • Hulio • Hyrimoz • Idacio
	• golimumab	• Simponi
	• certolizumab pegol	• Cimzia
	• etanercept	• Enbrel • Brenzys • Erelzi
	• infliximab	• Remicade • Avsola • Inflectra • Remsima • Renflexis
Anti-Inflammatory	• Sulfasalazine	• Salazopyrin • Azulfidine
	• 5-Aminosalicylic Acid (ASA)/mesalamine	• Pentasa
Anti-CD20	• Rituximab	• Rituxan • Ruxience • Riximyo • Truxima • Riabni
	• ocrelizumab	• Ocrevus
	• ofatumumab	• Kesimpta
IL-1 RA (interleukin-1 receptor antagonist)	• anakinra	• Kineret
	• canakinumab	• Ilaris
Anti-IL6	• tocilizumab	• Actemra
	• sarilumab	• Kevzara
Anti-IL12/IL23	• ustekinumab	• Stelara

Class	Generic Name(s)	Brand Name(s)
Anti-IL17	• secukinumab	• Cosentyx
	• ixekizumab	• Taltz
Anti-ILI7R	• brodalumab	• Siliq
Anti-BLyS	• belimumab	• Benlysta
Anti-IL23	• guselkumab	• Tremfya
	• risankizumab	• Skyrizi
Selective T-cell costimulation blocker	• abatacept	• Orencia
S1PR (sphingosine 1-phosphate receptor) agonist	• fingolimod	• Gilenya
	• siponimod	• Mayzent
	• ozanimod	• Zeposia
Phosphodiesterase inhibitors	• Apremilast	• Otezla
Anti-integrin	• vedolizumab	• Entyvio

Appendix B

Clinic Guide to Verifying Immunosuppressive Prescriptions for Second Doses of Imvamune®

The following information is guidance for vaccination clinics administering second doses of Imvamune® to individuals receiving immunosuppressive therapies who present a prescription of their medication (see Appendix A).

Step 1: Verify Prescription Details

- The individual should present a current prescription receipt from a pharmacy, or present a current medication bottle/package that includes the following information:
    - Date of prescription
        - To be considered current, the prescription should be prescribed or refilled within the past 6 months.
        - Active treatment for patients receiving B-cell depleting therapies (monoclonal antibodies targeting CD19, CD20 and CD22) includes patients who have completed treatment within 12 months.
    - Patients first and last name
        - The first and last name should be compared to a piece of identification.
    - Address and telephone number of the pharmacy

Step 2: Cross-Reference Drug Name

- Confirm that the drug name is listed in Table 2.
- Table 2 provides a list of immunosuppressive medications that qualifies individuals to receive a second dose.
    - This list may not be comprehensive. If an individual presents a prescription of a medication that is not listed in Table 2, they should be directed to their healthcare provider to receive a referral form/letter for a second dose of Imvamune®

Step 3: Administer Vaccine

- If the individual's prescription is deemed valid and the drug name is listed in the table below, a second dose of the Imvamune® vaccine can be administered and documented into Panorama.