

Smallpox and Monkeypox Vaccine (Live attenuated, non-replicating) IMVAMUNE® Supplier: Bavarian Nordic A/S

INDICATIONS:

- Post-Exposure Prophylaxis of select close contacts as determined by Medical Health Officer (MHO). The vaccine can be given up to 14 days after exposure; immunization within 4 days of exposure is necessary to prevent infection. Immunization 4-14 days following exposure may reduce severity of clinical manifestations.
- Pre-Exposure Prophylaxis may be considered per [Communicable Disease Control Manual, Chapter 1: Interim Guidance: Public Health Management of Cases and Contacts Associated with Monkeypox in the Community Settings](#) (refer to Pre-Exposure Prophylaxis).

The vaccine is not indicated for those with signs and symptoms of monkeypox.

The vaccine is not approved for use in those less than 18 years of age. ^A

DOSES AND SCHEDULE: ^B

Standard subcutaneous (SC) dose regimen: 2 doses given as 0.5 mL **SC**, at least 28 days apart.

Alternate subcutaneous (SC) and intradermal (ID) dose regimen:

- Dose 1 given as 0.5 mL **SC**
- Dose 2 given as 0.1 mL **ID**, at least 28 days after the first dose.

Immunocompetent individuals 18 years of age and older can be immunized using either the ID or SC administration route for the second dose. ^C Immunocompromised individuals (see [Appendix A](#)), individuals less than 18 years of age, and individuals of any age with a history of developing keloid scars, should be immunized using the standard SC dose regimen only.

ADMINISTRATION:

- No reconstitution required.
- For subcutaneous administration, administer the entire volume of the vial.
- For intradermal administration:
 - If the vial is used for multiple doses, it should be stored at +2°C to +8°C, and discarded after 6 hours following first puncture.
 - The preferred site for ID administration of IMVAMUNE® is the inner (volar) surface of the forearm. If the volar surface of the forearm is not an option (e.g., heavy scarring, bilateral amputation), the suprascapular areas may be used.
 - For ID administration of IMVAMUNE®, a white elevated wheal (bleb) 6-8 mm in size should appear. If an elevated wheal does not appear, repeat the procedure using an alternate site. For further information on ID administration, see [Appendix B – Administration of Biological Products](#), section 14.8 Intradermal Injections.

^A This vaccine may be considered for individuals less than 18 years of age if risk assessment deems that the benefits outweigh the potential risks for the individual, and if informed consent includes discussion about the absence of evidence on the use of this vaccine in this age group.

^B Immunocompetent individuals who have previously been vaccinated against smallpox should receive 1 dose for either pre or post-exposure prophylaxis. Individuals who are moderately to severely immunocompromised should receive 2 doses, regardless of previous smallpox vaccination.

^C In situations where individuals have received a first dose of IMVAMUNE® using an ID route, the dose should be considered valid.

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ADMINISTRATION (continued):

Storage and Handling:

- The vaccine will be shipped to health authorities at -20°C or at -80°C on dry ice for prepositioning and storage at freezer temperatures of -90°C to -70°C or -25°C to -15°C. Dry ice shipments must be handled by staff trained in management of this material (see [Dry Ice Handling Safety Training](#)). The vaccine can be stored frozen at -90°C to -70°C up until the expiry date stamped on the carton. If vaccine is stored at -25°C to -15°C, the expiry date is 3 months (91 days) from the date it is moved from -90°C to -70°C storage. Any time used for transport of the vaccine at -20°C is cumulative and needs to be subtracted from the 3 months (91 days) of allowable storage at -25°C to -15°C. Record the new expiry date on the carton.
- Once thawed, the vaccine can be stored in the refrigerator at +2°C to +8°C for up to two weeks (record the new expiry date on the vial prior to commencing refrigeration storage) and should be kept in the original packaging and protected from light.
- Do not refreeze thawed vials.
- If removing from freezer storage for use, thaw at refrigeration or room temperature. A vial of vaccine will take approximately 5 minutes to thaw at room temperature. Gently swirl vaccine upon thawing for at least 30 seconds to ensure homogeneity; **do not shake**.
- Once thawed, the vaccine will appear as a pale milky coloured homogeneous suspension. Inspect vial to confirm there is no foreign particulate matter. If any is observed do not administer the vaccine.

BOOSTER DOSES:

No booster doses are recommended at this time.

SEROLOGICAL TESTING:

Serological testing is not recommended before or after immunization.

CONTRAINDICATIONS:

1. History of anaphylactic reaction to a previous dose of the vaccine or to any component of the vaccine.

PRODUCT COMPONENTS:

Potential allergens: chicken protein, gentamicin, ciprofloxacin.

Other components: trometamol, sodium chloride, benzonase.

PRECAUTIONS:

- IMVAMUNE® may be considered for those with immunosuppression due to disease or treatment, and pregnant and lactating people, if a risk assessment deems that the benefits outweigh the potential risks for the individual, and if informed consent includes discussion about the limited data available on the use of IMVAMUNE® in these populations.
- The intradermal route of administration should not be used for those who are immunocompromised, individuals less than 18 years of age, and individuals of any age who have a history of developing keloid scars.

SPECIAL CONSIDERATIONS:

- IMVAMUNE® is a non-replicating live attenuated vaccine that contains genetically modified *orthopoxvirus* that has lost its ability to replicate in human cells.

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SPECIAL CONSIDERATIONS (continued):

- As IMVAMUNE® is a non-replicating live vaccine, a 4 week interval between administration of this vaccine and another live vaccine is not required. As data on co-administration of IMVAMUNE® and other vaccines are not available, it is recommended to not co-administer IMVAMUNE® with other vaccines, and wait for a period of at least 14 days between administration of IMVAMUNE® and another live or inactivated vaccine. The administration of IMVAMUNE® for post-exposure prophylaxis should not be delayed in an individual who has recently received another vaccine.
- Those who have recovered from laboratory confirmed monkeypox are assumed to have acquired immunity and vaccine is not indicated. The duration of protection following recovery from infection is unknown.
- This vaccine can be given any time before or after tuberculin skin testing.

ADVERSE EVENTS:

Local: pain, redness, induration, swelling, pruritus.

Systemic: fatigue, headache, myalgia, arthralgia, fever, chills, nausea, loss of appetite.

Most of these reactions are mild to moderate in intensity and resolve within 7 days of vaccine receipt. Local and systemic reactions are more common in people with atopic dermatitis.

In the one study ^A that examined reactogenicity after subcutaneous versus intradermal administration, moderate/severe measured erythema and/or induration was seen more frequently (95%) with ID injection compared to SC (58%), and the reactions lasted longer with ID group. In the ID group, 36% of recipients had mild injection site skin discoloration lasting 6 months or longer. The frequency of systemic adverse events did not differ among the two groups.

Cardiac adverse events such as myocarditis, pericarditis or any other type of cardiac inflammatory disease have not been clearly shown to be associated with use of IMVAMUNE®. However, cardiac adverse events are of interest given recognized association with smallpox vaccine. Recipients of IMVAMUNE® experiencing chest pain, shortness of breath or palpitations should be assessed for additional findings including troponin elevations and EKG abnormalities.

REFERENCES:

1. IMVAMUNE® [product monograph](#)
2. [National Advisory Committee on Immunization: NACI Rapid Response – Updated interim guidance on Imvamune® in the context of ongoing monkeypox outbreaks](#)

^A Frey SE, Wald A, Edupuganti S, Jackson LA, Stapleton JT, El Sahly H, et al. Comparison of lyophilized versus liquid modified vaccinia Ankara (MVA) formulations and subcutaneous versus intradermal routes of administration in healthy vaccinia-naïve subjects. *Vaccine*. 2015 Sep 22;33(39):5225,5234. doi: 10.1016/j.vaccine.2015.06.075

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Appendix A

Moderately to severely immunosuppressed includes those who:

- Have had a solid organ transplant and are taking immunosuppressive therapy (heart, lung, liver, kidney, pancreas or islet cells, bowel or combination organ transplant).
- Will have, are having, or are on active treatment for solid tumour or haematologic malignancies (like myeloma or leukemia):
 - Will have, are having, or in the last 12 months have received systemic treatment for a haematological malignancy, or in the last 24 months have received anti-CD20 or other B-cell depleting therapies for a haematological malignancy.
 - Will have, are having, or in the last 24 months have had a bone marrow, stem cell transplant or CAR-T or who are still taking immunosuppressive drugs.
 - Will have, are having, or in the last 6 months have received anti-cancer systemic therapy for solid tumours (including but not limited to cytotoxic chemotherapy; molecular targeted therapy; immunotherapy; monoclonal antibodies; bone modifying agents used in the setting of metastatic disease; high dose steroids e.g., equivalent to > 20 mg/day for more than 1 month but excluding patients only receiving hormonal or bone modifying therapy in the adjuvant setting).
 - Are planned for radiation, are having or will have had radiation in the last 3 months.
 - Have a diagnosis of CLL/SLL, myeloma/plasmacytoma, or low grade lymphoma.
- Prior AIDS defining illness or prior CD4 count $\leq 200/\text{mm}^3$ or prior CD4 fraction $\leq 15\%$ or any detectable plasma viral load since January 2021 or HIV infection and ≥ 65 years old or perinatally acquired HIV infection.
- Are on active treatment with the following categories of immunosuppressive therapies:
 - In the last 2 years, been treated with anti-CD20 agents, B-cell depleting agents or similar therapeutic agents.
 - In the last 3 months, been treated with biologic agents that are significantly immunosuppressive, oral immune-suppressing drugs, steroids (orally or by injection >14 days), immune-suppressing infusions/injections or intermittent high dose steroids administered as immune suppression prior to intravenous enzyme replacement treatment.
- Have combined immune deficiencies affecting T-cells, immune dysregulation (particularly familial hemophagocytic lymphohistiocytosis) or those with type 1 interferon defects (caused by a genetic primary immunodeficiency disorder or secondary to anti-interferon autoantibodies).
- Have a moderate to severe primary immunodeficiency which has been diagnosed by an adult or pediatric immunologist and requires ongoing immunoglobulin replacement therapy (IVIG or SCIG) or the primary immunodeficiency has a confirmed genetic cause (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome).
- On dialysis (hemodialysis or peritoneal dialysis) or have stage 5 chronic kidney disease (eGFR <15 mL/min) or have glomerulonephritis and receiving steroid treatment.