
NITAG support hub: Vaccinology webinar series for NITAGs in Africa

SAGE recommendations for mpox

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28 August 2024



Mpox vaccine and immunization recommendations

- In response to the global mpox outbreak, interim guidance on mpox vaccines and immunization was endorsed by SAGE and published in November 2022
- In the last year, additional epidemiological data has been obtained from the African setting
- New information has become available regarding the safety and vaccine effectiveness of MVA-BN
- SAGE considered this for the 2024 updated mpox vaccine and immunization recommendations
- These updated mpox vaccine recommendations are now published in a position paper which combines SAGE endorsed smallpox vaccine recommendations developed in October 2023

Smallpox and mpox vaccine position paper [WER9934-eng-fre.pdf \(who.int\)](#)

Recommendation mpox outbreak response¹

- Vaccination is **recommended for persons at high risk of exposure to mpox in an outbreak**. The identification of populations at risk of exposure is limited in some settings by currently available epidemiological data. This is particularly the case for communities affected by zoonotic transmission. In studies involving men who have sex with men, pre-exposure vaccination with one or two doses of smallpox/mpox vaccine was demonstrated to be effective against mpox. Effectiveness of post-exposure vaccination is less certain, which may be linked to the predominantly sexual mode of transmission in available studies. To allow the greatest flexibility with respect to local risk assessment, varied modes of transmission and response options, populations to consider for vaccination may include:
 - **based on local epidemiology**, members of a geographically defined area or community (e.g. village), including children, with a documented high risk of exposure to mpox;
 - sex workers; gay, bisexual or other men who have sex with men (MSM) with multiple sexual partners; or other individuals with multiple casual sexual partners;
 - **health workers at risk of repeated exposure**; clinical laboratory and health care personnel performing diagnostic testing for mpox or providing care, and outbreak response team members (as designated by national public health authorities).
 - **contacts of persons with mpox**, ideally within four days of first exposure.² Contacts may include children, others in the household or in congregate settings (such as prisons, schools, health facilities or residential facilities)

1. *Outbreak definition: occurrence of two or more laboratory confirmed (or one laboratory confirmed and one or more epidemiologically linked cases) of mpox in nationally or locally defined geographic areas*

2. *Criteria to define risk of exposure in this context include e.g. direct skin-to-skin physical contact, contact with contaminated materials such as clothes or bedding. Vaccination ideally up to 14 days in the absence of symptoms.*

Choice of vaccines for immunocompetent non-pregnant individuals

- WHO recommends that for immunocompetent non-pregnant individuals, non-replicating vaccine (MVA-BN), minimally replicating vaccines (LC16m8), replicating cell-culture derived vaccinia-based vaccines (e.g. ACAM2000) or equivalent vaccines that meet WHO standards for quality, are appropriate for use.
- Specific considerations, including potential off-label use, apply as to vaccine choice for special population groups (see recommendation on vaccine choice for special populations).

Choice of vaccine for special populations - infants, children and adolescents

- For infants, children and adolescents, where consideration is given to vaccination, non-replicating (MVA-BN) or minimally replicating (LC16m8) vaccines may be used.
 - LC16m8 is approved for use in children in Japan. However, LC16m8 is contraindicated in pregnancy and in immunocompromised children and adolescents, including in uncontrolled advanced HIV.
 - While MVA-BN is currently not licensed for persons under 18 years old, this vaccine may be used in infants, children and adolescents when the benefits of vaccination outweigh the potential risks in the context of an outbreak. The use of MVA-BN in children constitutes an “off-label” product use.
 - Replicating vaccine (such as ACAM2000) should not be used in infants.
 - WHO recommends further collection of data on vaccine safety and effectiveness for these populations.

Choice of vaccine for special populations - pregnancy

- During pregnancy, where consideration is given to vaccination, non-replicating vaccine (MVA-BN) should be used. Replicating vaccine (such as ACAM2000) and minimally replicating vaccine (such as LC16m8) should not be used in pregnancy. Administration of MVA-BN in pregnancy constitutes “off-label” use.

Choice of vaccine for special populations – immunocompromised persons

- For immunocompromised individuals for whom replicating (such as ACAM2000) or minimally replicating (LC16m8) vaccine is contraindicated, non-replicating vaccine (MVA-BN) should be used; likewise for individuals for whom there are warnings or precautions because of immunosuppressive therapies or proliferative skin conditions (e.g. atopic dermatitis), non-replicating (MVA-BN) vaccine should be used.
- Immunocompromised persons include those with active cancer, transplant recipients, immunodeficiency, and active treatment with immunosuppressive agents. They also include people living with HIV with a current CD4 cell count of <200 cells μ l.

Vaccination schedules and dosing

Based on the risk profile and the available vaccine data, WHO recommends “off-label” use of a single dose or intradermal fractional dosing* of MVA-BN in supply-constrained outbreak situations. WHO emphasizes the need to collect further data on vaccine safety and effectiveness in these circumstances.

*one fifth of a dose (0.1mL) administered intradermally

Vaccination in previously vaccinated individuals

The duration of protection of vaccinia-based mpox vaccines is not fully characterized and may vary between vaccine products. WHO recommends that individuals who are eligible for vaccination should be vaccinated irrespective of documented previous smallpox vaccination and/or visible smallpox vaccine scar. For individuals previously vaccinated with mpox vaccines, an individual benefit-risk assessment should be done.

Thank you

Mpox vaccine effectiveness: A systematic review and meta-analysis

PREVENTIVE VACCINATION

- **VE Estimate for 1-dose of MVA-BN: 76% (95%CI 65%-86%)**
 - *Relative stability of estimate with removal of poor-quality studies*
- **VE Estimate for 2-dose of MVA-BN: 82% (95%CI 72%-92%)**
 - *Relative stability of estimate with removal of poor-quality studies*
 - *Prioritize vaccination prior to exposure for at-risk individuals*

POST EXPOSURE PROPHYLAXIS

- **VE Estimate PEP with MVA-BN: 20% (95%CI -24%-64%)**
 - *Challenging to measure VE and obtain appropriate control group*
 - *Low VE may in part be due to sexual transmission in study group*
 - *If PEP used, rapid access to vaccination recommended (<4 days)*
- GRADE with very low confidence for all estimates

Mpox systematic review on vaccine safety

- All mpox vaccines give local and systemic adverse events
- ACAM2000 (second generation vaccines) has a higher SAE and myocarditis risk compared to third generation vaccines (LC16, MVA-BN)
- LC-16 is approved for use in children in Japan with a good safety profile (use in 50,000 children, no serious adverse events).
- MVA-BN is licensed for persons 18 and older.
 - Limited data on MVA-BN use in children (studies in 159 children, use in a further 1003 children) show a good safety profile (no serious AE).
 - EBV vaccine (MVA-BN-filo) demonstrates a good safety profile (n= 52,229) and is licensed for use in children aged 1 and older.
- Graded certainty of evidence is low to very low

Preventive use of mpox vaccines (outside of an outbreak)

Primary preventive vaccination is recommended for:

- Laboratory personnel working with orthopoxviruses

The duration of protection of mpox vaccines is not fully characterized. Therefore, periodic revaccination should be considered for individuals who are at high risk of exposure to more virulent orthopoxviruses (e.g. variola virus, monkeypox virus, cowpox virus, vaccinia virus and/or others as appropriate). This may be as often as every 2 to 5 years for laboratory workers at highest risk of exposure, as practiced in the two authorized WHO Collaborating Centres for variola virus research, or less frequently in other settings, according to the latest available information on duration of protection for the vaccines used.