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Belgian Vaccination Strategy against Human Mpox Virus

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ADVISORY REPORT OF THE SUPERIOR HEALTH COUNCIL no. 9900

Belgian Vaccination Strategy against Human Mpox Virus

In this scientific advisory report, which offers guidance to public health policy-makers, the Superior Health Council (SHC) of Belgium provides **updated recommendations** on the Belgian vaccination strategy against Human Mpox Virus (HMpoxV) with third generation MVA-BN (Modified Vaccinia Ankara - Bavarian Nordic; Imvanex®-Imvamune®-Jynneos®)

This version was validated by the NITAG on January 29th, 2026
This version was validated by the Board on March 4th, 2026[1]

I INTRODUCTION

The Superior Health Council (SHC)'s August 2022 monkeypox (Mpox) vaccination guidelines (SHC 9720 and 9727) require updating following the emergence and spread of clade Ib/sh2023, which has demonstrated autochthonous transmission in European countries.

The Sciensano Risk Assessment Group (RAG) in November 2025 identified cases in Spain, Italy, Portugal, and the Netherlands without travel links to endemic countries, marking the first evidence of possible introduction into sexual networks beyond previously documented household transmission.

Effective vaccination strategies can assist to control spread, especially among high-risk populations. Here we present updated Belgian guidelines recommending targeted pre- and post-exposure prophylaxis using the third-generation Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN) vaccine.

Pre-exposure prophylaxis (PrEP) targets persons with frequently changing sexual partners (including men who have sex with men (MSM), sex workers, and transgender persons). Post-exposure prophylaxis (PEP) provides vaccination for close contacts of confirmed, probable, or suspected cases, preferably within a four-day window.

Pre-exposure vaccination shows substantial effectiveness against symptomatic infection and hospitalization, with a favourable safety profile across diverse populations. Antibody concentrations decline following vaccination. Whether clinical protection persists long-term remains uncertain.

Booster doses are not currently recommended given insufficient evidence of clinical benefit, though studies are ongoing.

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[1] The Council reserves the right to make minor typographical amendments to this document at any time. On the other hand, amendments that alter its content are automatically included in an erratum. In this case, a new version of the advisory report is issued

II CONCLUSIONS AND RECOMMENDATIONS

1 Place of administration

All vaccinations administered at HIV Reference Centers (12 sites) and/or travel clinics attached to HIV Reference Centers or community-based organizations (CBOs) dedicated to sex workers communities.

2 Summary table

Population Category	Eligibility Criteria	Remarks
PRE-EXPOSURE PROPHYLAXIS (PrEP) - PRIMARY PREVENTION		
Persons with frequently changing sexual partners	• HIV-positive (preferably with CD4 > 200 cells/mm³ and undetectable viral load) • HIV PrEP users • Multiple/changing sexual partners • Commercial sex work (all genders) • Transgender persons with risk behaviours Self-attestation model (no documentation required)	• Integrate into periodic clinic visits or CBOs dedicated to sex workers
Deploying to endemic regions (*): Humanitarian and health care workers	**After individual/group risk assessment:** • Direct patient care with suspected/confirmed cases • Clinical care of Mpox patients • Uncontrolled hygiene conditions • Laboratory workers with high risk of exposure	• Start ≥ 6 weeks pre-departure; peak immunity 2 weeks post-dose 2
Travelers to endemic regions (**) *(Visiting friends/relatives (VFR), general tourism)*	**Individual case-by-case** ONLY if infectiologist deems vaccination "absolutely essential" based on: • Individual medical risk factors (severe immunosuppression, inflammatory skin conditions, pregnancy) • Unknown/poorly controlled local conditions with high exposure risk	• Start ≥ 6 weeks pre-departure; peak immunity 2 weeks post-dose 2
Travelers anticipating high-risk sexual activities (***)	• Sex tourism to any destination • Multiple sexual partners expected during travel • Commercial sex venues abroad • Sex-related events during travel *Regardless of destination if high-risk sexual practices anticipated*	• Start ≥ 6 weeks pre-departure; peak immunity 2 weeks post-dose 2
POST-EXPOSURE PROPHYLAXIS (PEP) - OUTBREAK RESPONSE - Preferably within 4 days after exposure (****)		
Close contacts of confirmed/probable/suspected cases	**Exposures:** • Sexual contact in past 2 weeks • Household/close contact • Direct skin contact with lesions **Vaccinate before laboratory confirmation of Mpox in index case if highly likely in index case**	• Complete series
Immunocompromised contacts	• HIV with low CD4 (< 200 cells/mm³) • Active immunosuppressive therapy • Organ transplant recipients	• Full 0.5 mL dose via subcutaneous route • Complete series

Pregnant contacts	• Any trimester • Pregnancy NOT an absolute contraindication, theoretically safe based on non-replicating platform, though human data limited	• Counsel on safety data • Risk-benefit assessment
Healthcare workers with documented exposure	• Unprotected contact with lesions/fluids • Percutaneous injury (e.g. needlestick injury after lesion aspiration) • Direct contact between unprotected mucous membranes (eyes, mouth, nose) and patient bodily fluids • PPE breach during care	• Document exposure details
SPECIAL POPULATIONS & CONSIDERATIONS		
Children & adolescents (*****)	• Post-exposure prophylaxis • Case-by-case for pre-exposure	**Schedule same as adults:** • 0.5 mL subcutaneous • Two-dose series
Booster doses	• Protection against hospitalisation & systemic symptoms persists > 24 months, however, evidence of antibody waning	• No booster recommended, insufficient data on booster benefit to support routine use. Reassessment planned as further evidence emerges.

(*) Endemic regions or high-risk regions include the following destinations: the Democratic Republic of Congo (DRC), Burundi, the Central African Republic, Rwanda, and Uganda.

(**) Geographic focus on endemic regions applies to general travelers, or VFR without specific sexual risk behaviors.

(***) Travelers anticipating high-risk sexual activities represent the same epidemiological risk group as domestic MSM with changing partners, maintaining exposure risk regardless of destination.

(****) PEP should ideally be given within 4 days, while from 4 to 14 days, PEP may reduce severity of disease.

(*****) Ages 12 - 17: EMA-approved (September 2024). Ages 2 - 11: EMA approval anticipated 2026; currently available for post-exposure prophylaxis case-by-case only. Ages < 2: Off-label use only in exceptional circumstances pending trial data (ongoing DRC trial NCT06844487).

3 Summary notes on vaccine

MVA-BN is a live, highly attenuated, replication-deficient vaccinia vaccine, safe for immunocompromised persons

3.1 Administration

Subcutaneous (SC): Two doses of 0.5 mL administered subcutaneously in the upper arm.

Intradermal (ID): Two doses of 0.1 mL (one-fifth standard dose) administered intradermally.

While **minimum interval is 28 days**, intervals of 2 - 3 months (or longer) between doses may improve immune response duration and should be considered when feasible, particularly for persons without immediate exposure risk.

Intradermal indication: Intradermal administration is used during vaccine supply constraints in immunocompetent individuals only, requiring healthcare professionals experienced in intradermal vaccine technique and use of low-volume syringes to maximize dose withdrawal.

3.2 Contraindications

Severe allergic reaction to previous MVA-BN dose or hypersensitivity to the active substance, any excipients, or trace residues (chicken protein, benzonase, gentamicin, ciprofloxacin).

No other absolute contraindications (pregnancy, immunosuppression, HIV are NOT contraindications)

III METHODOLOGY

The Board and the co-presidents of the National Immunization Technical Advisory Group (NITAG) identified the necessary fields of expertise. An *ad hoc* working group was set up which included, among others, experts in travel medicine, paediatrics, infectiology and epidemiology. The experts of this working group provided a general and an *ad hoc* declaration of interests and the Committee on Deontology assessed the potential risk of conflicts of interest.

This advisory report is based on a review of the available scientific literature published in both scientific journals (peer-reviewed), preprint article and reports from national (RAG-RMG) and international (WHO; ECDC; CDC; EMA; FDA; others NITAGs) organisations competent in this field as well as on the opinion of the experts.

Once the advisory report was endorsed by the *ad hoc* working group and NITAG, it was ultimately validated by the Board on March 4th, 2026.

This document was developed with the support of artificial intelligence tools, used under human supervision, and underwent several cycles of expert review and validation.

Keywords

Keywords	***Sleutelwoorden***	***Mots clés***	***Schlüsselwörter***
Prevention	*Preventie*	*Prévention*	*Verhütung*
Vaccination	*Vaccinatie*	*Vaccination*	*Impfung*
Men having Sex with Men, MSM	*Mannen die Seks hebben met Mannen, MSM*	*Hommes ayant des rapports Sexuels avec des Hommes, HSH*	*Männer, die Sexualverkehr mit Männern haben, MSM*
Multiple sexual partners	*Meerdere seksuele partners*	*Partenaires sexuels multiples*	*Mehrere Sexualpartner*
High Risk Contacts, HRC	*Contacten met hoog risico*	*Contacts à haut risque*	*Kontakte mit hohem Risiko*
Smallpox	*Pokken*	*Variole*	*Pocken*
Monkeypox	*Apenpokken*	*Variole du singe*	*Affenpocken*

List of abbreviations used

CDC	Centers for Disease Control and Prevention – US
CBO	Community-Based Organisations
ECDC	European Centre for Disease Prevention and Control - EU
EMA	European Medicines Agency - EU
FDA	Food and Drug Administration - US
GMT	Geometric Mean Titers
HIV	Human Immunodeficiency Virus
hMpoxV	Human Monkeypox Virus
HRC	High Risk Contacts
ID	Intradermal Injection
Mpox	Monkeypox
GBMSM	Gay, Bisexual and other Men-who-have-Sex-with-Men
MVA-BN®	Modified Vaccinia Ankara - Bavarian Nordic; Imvanex®-Imvamune®-Jynneos®

NaTHNaC	National Travel Health Network and Centre
NITAG	National Immunization Technical Advisory Group
PCR	Polymerase Chain Reaction
PEP(V)	Post-Exposure Prophylaxis (Vaccination)
PrEP	Pre-Exposure Prohylaxis (VIH)
QALYs	Quality-Adjusted Life Years
RAG	Risk Assessment Group - BE
RMG	Risk Management Group - BE
SC	Subcutaneous Injection
SHC	Superior Health Council - BE
STI	Sexually Transmitted Infection
UAE	United Arab Emirates
UKHSA	UK Health Security Agency - UK
VE	Vaccine Effectiveness
VFR	Visiting Friend and Relative
WHO	World Health Organization - World

IV ELABORATION AND ARGUMENTATION

1 Mpox disease and hMpoxV: General Introduction

Mpox is an infectious disease caused by the mpox virus, a double-stranded DNA virus belonging to the Orthopoxvirus genus in the Poxviridae family, closely related to the virus that caused smallpox. The virus exists in two major clades with distinct geographic distributions: clade I (historically endemic in Central Africa) and clade II (West African origin) (Srivastava et al., 2025).

Clade Ib emerged in 2024 with approximately 149 nucleotide changes and 54 % increased genetic variation compared to clade I. International spread to multiple continents occurred through cross-border sexual networks and subsequent household (Srivastava et al., 2024). Transmission mainly occurs through direct contact with infected skin lesions or body fluids, including sexual contact; less frequently, transmission has been documented through fomites (contaminated materials), respiratory droplets, and consumption of contaminated meat from infected animals (Srivastava et al., 2024).

Mpox incubation period (time from infection to symptom onset) typically ranges from 7 - 14 days, with a median of 8 - 9 days based on contemporary European outbreak data (McFarland et al., 2023). The incubation period can extend from 5 - 21 days, though approximately 5 % of cases may exceed the commonly used 21-day monitoring period (McFarland et al., 2023).

Mpox transmission does not occur during the early incubation period, though viral shedding enabling pre-symptomatic transmission may begin 1 - 4 days before symptom onset (Brosius et al., 2023). Contact tracing studies from the 2022 outbreak demonstrated that symptomatic cases were the primary source of transmission. In UK households, sexual contact with symptomatic index cases conferred an 11-fold increased risk of infection (adjusted OR 11.0, 95 % CI 5.5 - 22, p<0.001), with an overall secondary attack rate of 4 % (60/1,526 household contacts) (Packer et al., 2024). Among 13 case-contact pairs analysed, only 4 had sufficiently reliable patient identifiers for transmission timing assessment. Three of these 4 pairs showed pre-symptomatic transmission up to 4 days before symptom onset (Ward et al., 2022), suggesting transmission before lesion recognition rather than truly asymptomatic spread.

Prospective screening of 1,159 MSM attending sexual health services in England detected mpox virus in only 0.17 % (2/1,159), coinciding with declining case numbers, suggesting asymptomatic infections were not sustaining transmission (Pitt-Kendall et al., 2023). While retrospective studies in Belgium identified asymptomatic PCR-positive individuals with replication-competent virus (3/224 samples) (De Baetselier et al., 2022), no outbreak investigations documented transmission chains originating from truly asymptomatic cases. US CDC concluded that "no cases of transmission have been definitively linked to exposure to infected people who never developed signs or symptoms of illness." (*Science Brief: Detection and Transmission of Mpox Virus | Mpox | Poxvirus | CDC*, n.d.)

Mpox typically presents as a self-limited illness lasting 2 - 4 weeks, with symptoms including fever, headache, myalgia, lymphadenopathy, and a characteristic vesiculopustular rash that progresses from macules to pustules before crusting. The 2022 - 2024 outbreaks, primarily involving clade IIb, demonstrated atypical clinical presentations with genital and perianal lesions, often without preceding systemic symptoms, particularly among men who have sex with men (Yadav et al., 2025). Severe disease occurs predominantly in immunocompromised populations, particularly persons living with HIV and low CD4 counts, while children and pregnant women in low-income countries face increased risk for complications and mortality (Huhn et al., 2005; Nachega et al., 2024).

Mpox poses a substantial risk to pregnancy outcomes. Evidence remains limited but growing. A pooled prospective cohort from the Democratic Republic of Congo followed 89 pregnant women with PCR-confirmed Clade I mpox; 69 had documented pregnancy outcomes (Hasivirwe Vakaniaki et al., 2025). Among these 69 women, 35 (51 %, 95 % CI 38 – 63 %) experienced adverse outcomes: 31 fetal losses (16 spontaneous abortions, 4 missed abortions, 11 stillbirths) and 4 congenital infections (one neonatal death). Adverse outcome rates varied by trimester: first trimester 94 % (17/18), second trimester 59 % (13/22), third trimester 17 % (5/29). Mpox virus DNA was detected in 9 of 12 (75 %) placental swabs tested, confirming vertical transmission capacity.

A systematic review of Clade IIb data identified 12 documented pregnancies between 6 - 31 weeks' gestation during the 2022 - 2023 outbreak; half ended in intrauterine fetal death (Sanchez Clemente et al., 2024). High viral loads (10^6 copies/mL) in fetal and maternal-fetal interface tissues demonstrate efficient placental transmission. Macaque models confirm vertical transmission occurs 6 - 14 days post-maternal infection, preceding fetal demise (Nachega et al., 2024). For historical context, smallpox data from 830 pregnant patients documented 39.9 % (95 % CI 36.5 - 43.2) miscarriage or premature birth rates and 34.3 % (95 % CI 31.4 - 37.1) maternal case fatality (Nishiura, 2006), suggesting orthopoxvirus pregnancy complications represent a class effect.

Treatment remains primarily supportive, including symptom management and prevention of secondary bacterial infections (*Mpox*, n.d.-a; Titanji et al., 2024). Antivirals such as tecovirimat, brincidofovir, and cidofovir have been used under compassionate use protocols for severe cases or high-risk patients. Recent randomized controlled trials (STOMP for clade II, PALM007 for clade I) demonstrated that tecovirimat monotherapy was safe but did not reduce time to lesion resolution compared to placebo ("Tecovirimat for Clade I MPXV Infection in the Democratic Republic of Congo", 2025; *Tecovirimat Is Safe but Ineffective as Treatment for Clade II Mpox | National Institutes of Health (NIH)*, n.d.). Mechanistic studies confirm tecovirimat does not reduce infectious viral shedding from lesions, with viable virus persisting beyond two weeks of treatment (Hurst et al., 2025).

On the long-term effects of mpox infections, a recent cohort study showed that persistent scarring affects approximately one-third of mpox patients at 24 months post-infection, underscoring that preventing infection carries clinical importance beyond reducing severe disease (Van Dijck et al., 2025).

Modelling of the 2022 clade IIb outbreak in European MSM demonstrated that infection-derived immunity contributed minimally to outbreak control (Hvid et al., 2025). The model, which incorporated survey data on sexual behaviour and the heterogeneous nature of sexual contact networks, revealed a marked decrease in serial interval throughout the epidemic that reflected substantial increases in self-isolation behaviour among infected persons. This behavioural adaptation proved sufficient to explain early epidemic control independent of immunity accumulation. The analysis confirmed that while adaptive behaviours curtailed the initial outbreak, the European MSM population remains protected primarily through vaccine-induced immunity rather than natural infection, underscoring vaccination's continued importance despite reduced transmission intensity.

2 Target groups for vaccination

2.1 Primary risk group for targeted Mpox vaccination: Persons with frequently changing sexual partners

2.1.1 Epidemiology

Historical international outbreaks of mpox were the result of zoonotic, household and, in rare cases, hospital-based transmission ($R_0<1$) (Mitjà et al., 2022). These outbreaks were typically self-limiting and did not lead to epidemics. However, the 2022 clade IIb pandemic was characterised by spread through sexual contact networks among MSM. Epidemic modelling suggests that its spread could be explained by heavy-tailed sexual contact networks, a heterogenous network in which a subset of individuals have a disproportionately higher number of contacts (i.e. superspreaders) (Pekar et al., 2025).

In Belgium, this epidemic led to 790 confirmed mpox infections in 2022 (*Mpox (Apenpokken) - Epidemiologische Situatie | Sciensano.Be*, n.d.). Since then, there have been sporadic cases of Mpox but without a subsequent outbreak. From January to October 2025, there were 59 cases, with the majority transmitted through sexual networks: 71 % MSM (30/42 with documented sexual behaviour), 83 % sexually acquired, 10 % HIV positive (4/38 with known serostatus) and 37 % PrEP users (15/41 with available data). PrEP users' overrepresentation among cases (37 %) compared to their estimated 1 - 2 % prevalence in the general MSM population quantifies this cohort's elevated exposure risk.

2.1.2 Population immunity

Immunity against (severe) disease can be acquired through 1) previous mpox infection, 2) recent mpox vaccination or 3) historical smallpox vaccination (people born before 1976). Since 2022, more than 900 mpox infections have occurred and approximately 1,500 vaccines administered (2-dose regimen: 550 in Belgium and 1,000 in France).

Unpublished data from the 2024 European MSM and trans people Internet Survey (EMIS) indicate that approximately 24 % of Belgian respondents had received two-dose mpox vaccination. However, due to convenience sampling, this percentage may be biased and overrepresent the level of vaccination uptake in this population group. (Aphami et al., 2025; De Vos et al., 2024; Threat Assessment Brief: Detection of Autochthonous Transmission of Monkeypox Virus Clade Ib in the EU/EEA, n.d.)
Nonetheless, a seroprevalence study among PrEP users at the Institute for Tropical Medicine detected approximately 50 % orthopoxvirus IgG seropositivity (comprising natural infection and vaccination) after the clade IIb 2022 epidemic. However, there are limitations to generalize these results as humoral immunity is not the sole correlate of protection, immunity may wane over time, and the single center study may not be representative at the national level (RAG, Sciensano).

Unpublished data from Sciensano (2022 – 2025) identified 43 breakthrough infections post-vaccination (minimum one-dose). Compared to non-vaccinated cases, the breakthrough cases were more often immunocompromised (7.0 % vs 3.6 %), but HIV seropositivity was similar (19 % vs 22 %), and none were hospitalized for treatment (compared to 4.4 % among non-vaccinated mpox cases). Post-2022 epidemic breakthrough infections occurred among 22 of 126 cases (17 %). International studies identified that breakthrough infections have accounted for 29 - 37 % (two-dose) and 10 – 11 % (one-dose) of post-epidemic mpox cases, but with a lower risk of severe disease compared to non-vaccinated cases (Latham et al., 2025; Charles et al., 2023).

2.1.3 Transmission dynamics

Mathematical modelling assessed the importance of heterogeneity in transmission risk. R_0 was only sufficiently high for epidemic expansion (R_0>1) among gay, bisexual MSM subgroups with the highest sexual partner rate (R_0 1.94, 95 % CI 1.82 - 2.19), with most mpox cases (> 80 %) either occurring within this subgroup or resulting from contact with this subgroup (Zhang et al., 2024). A (pre-print) modelling study estimated that targeted vaccination of the most sexually active subgroup, even with a modest increase in vaccination uptake, had the largest impact on reducing the probability of an outbreak (Prasse et al., 2025).

The Netherlands implemented this strategy with quantified eligibility (≥ 10 partners per six months) (Adam et al., 2024), while France adopted qualitative "multiple partners" criteria (*Service Public*). UK established a routine pre-exposure programme through sexual health services from August 2025 (GOV.UK).

Belgium's 10,100 registered PrEP users attending HIV reference centers quarterly provide existing infrastructure for vaccine delivery with minimal organizational expansion. Sex workers (estimated 25,000 - 30,000 nationally) and MSM living with HIV (4263 aged 20 - 50 years old in 2024) represent additional priority populations, though accessing sex workers presents greater implementation challenges than the PrEP cohort already engaged in regular clinical follow-up (RAG, Sciensano). In this context, strengthened collaboration with community-based organisations (CBOs) working with sex workers could substantially facilitate outreach and support vaccination uptake within this group.

2.2 Other risk groups targeted for Mpox vaccination

2.2.1 Occupational health risk: health care workers in Belgium

Recent nosocomial transmission outside endemic areas has been rare and primarily associated with sharps injuries and breaches in transmission-based precautions (Zachary et al., 2023). Occupational mpox transmission to healthcare workers remains rare in well-resourced settings when standard precautions are maintained (Safir et al., 2023; Zachary et al., 2023). However, confirmed occupational infections through needlestick injuries during lesion aspiration occurred by late 2022 (Carvalho et al., 2022; Y. Choi et al., 2023; Safir et al., 2023).

International consensus excludes most healthcare workers from routine vaccination, limiting recommendations to laboratory personnel handling orthopoxviruses and infectious disease unit staff. In African outbreak settings, nosocomial transmission increased due to inadequate PPE access and infection prevention failures (CDC; Ebede et al., 2025).

2.2.2 Humanitarian personnel

France recommends vaccination for health professionals and humanitarian workers traveling to regions with clade I transmission, particularly DRC and Great Lakes neighbors (*Mesures de Prévention)*. Canada strongly recommends completing two-dose vaccination before international deployment to support mpox outbreak response (Murray, 2025; Canada.Ca).

Risk assessment should evaluate: direct patient care responsibilities, lesion sampling or laboratory duties, shared accommodation with affected populations, PPE availability, outbreak intensity at deployment site, and mission duration. Brief technical consultations involving limited patient contact present different exposure profiles than sustained field assignments with repeated community contacts or clinical duties.
Unpublished data from a US CDC trial in the DRC assessing the effectiveness of MVA-BN vaccination among healthcare professionals working in affected mpox regions found that over a longer follow-up period of five years, there were sporadic cases of post-vaccination infections. Based on these findings, CDC does not recommend booster vaccination for healthcare workers and is following up the duration of protection over a seven-year period. (*Interim Clinical Considerations for Use of Vaccine for Monkeypox Prevention in the United States* | *Monkeypox* | *CDC*, n.d.)

This individualized approach recognizes that deployment label alone fails to predict transmission risk. A two-week clinical rotation in a crowded DRC health facility presents higher exposure than a six-month advisory role in a capital city administrative office.

2.2.3 Travel

Travel-Associated Transmission Patterns

Mpox transmission during international travel follows the same pattern as domestic transmission: sexual contact drives the outbreak. General travelers without high-risk sexual exposures face negligible acquisition risk, regardless of destination. The 70+ confirmed travel-associated clade I cases detected globally through January 2025 almost uniformly involved individuals whose risk profile matched domestic high-risk groups, not incidental contact during tourism or family visits.

Travelers at elevated risk share the same characteristics as high-risk populations within Belgium: multiple sexual partners, commercial sex, attendance at sex venues or events, or engagement with sex worker networks. Geographic destination amplifies or attenuates this baseline behavioral risk depending on local circulation. Sex tourism destinations and countries with ongoing outbreaks (DRC, neighboring Great Lakes countries, and increasingly transit hubs like United Arab Emirates (UAE) increase probability of encountering an infected partner.

By March 2025, 28 countries reported travel-associated clade Ib cases, with Uganda identified as the most frequent source country globally, followed by UAE (UKHSA, n.d.). Of 114 clade Ib cases reported to WHO through October 2025, 76 represented primary importations and 15 generated 38 secondary cases without tertiary spread. Belgium reported 5 imported clade Ib cases through October 2025, with one generating self-limited household transmission without introduction into sexual networks, demonstrating successful containment despite historical ties to Central Africa that create distinct importation pathways (RAG, Sciensano; UKHSA, n.d.).

The UAE pattern revealed unexpected transmission complexity. Although UAE reported its first confirmed clade Ib case in February 2025 (an adult with recent Uganda travel, symptom onset January 11), seven to eight travel-associated cases across five countries (Thailand with four cases, India, Pakistan, Oman, and China) reported UAE exposure during preceding months (Pareek et al., 2025; Satheshkumar et al., 2025). Phylogenetic analysis demonstrated these UAE-linked cases formed a monophyletic cluster, with sequences indicating presence of similar strains in both Uganda and UAE around September - October 2024, suggesting undetected transmission chains existed before case recognition (Mpox: Multi-Country External Situation Report No.45; Satheshkumar et al., 2025).

Saudi Arabia reported nine laboratory-confirmed cases in 2024 without deaths, mostly travel-linked to endemic areas, with clade IIb circulation confirmed through genomic sequencing. Sustained human-to-human transmission occurred domestically without documented secondary cases (Al Awaidy et al., 2025). Pakistan detected three cases with travel histories to both Saudi Arabia and UAE, supporting Middle Eastern hub transmission risk (Al Awaidy et al., 2025).

Belgium should offer pre-travel vaccination selectively to travelers whose planned activities place them at elevated risk, not based on destination alone. Travel clinics should assess:

- Anticipated sexual contact with local residents or travelers from endemic areas.
- Engagement with commercial sex or sex venues at destination.
- Prolonged close household contact in areas with active community transmission (VFR travelers).
- Medical risk factors that increase severity (immunocompromise, inflammatory skin conditions).

CDC recommends completing the two-dose series with first dose at least six weeks pre-departure, creating logistical barriers for travelers with shorter planning horizons. Single-dose vaccination offers partial protection (~75 % effectiveness) and may be appropriate for last minute travelers meeting risk criteria.

Geographic scope beyond traditional endemic zones

Travel risk assessment should account for evolving transmission geography. The UAE pattern demonstrated that undetected chains can establish in transit countries before case recognition: seven to eight cases across five countries had UAE exposure during months preceding UAE's first confirmed case. Belgium's historical ties to Central Africa create distinct importation pathways, but indirect routes through Middle Eastern or Asian hubs warrant consideration when assessing travelers' exposure history and post-travel monitoring.

2.2.4 Pre-deployment and Travel Vaccination Timing

Travelers to mpox-endemic areas should initiate vaccination at least 6 weeks before departure to complete the two-dose series and achieve peak immunity. The standard regimen requires doses administered 28 days apart (minimum 4 weeks), with optimal antibody responses achieved approximately 14 days after the second dose. This timing ensures travellers receive dose 1 at departure minus 6 weeks, dose 2 at departure minus 2 weeks, and reach presumed optimal protection at time of travel.

Travelers unable to complete the series before departure should receive at least one dose, as partial immunity provides meaningful risk reduction during exposure. Single-dose recipients departing before completing the series achieve partial protection (effectiveness 36 – 75 % versus 66 – 89 % for two doses) and should complete the second dose upon return.

3 Vaccination

3.1 Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN)

Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN) represents a third-generation smallpox vaccine developed by Bavarian Nordic A/S (Kvistgård, Denmark) using a replication-deficient vaccinia virus strain produced in chick embryo cells. The vaccine received initial European Medicines Agency (EMA) approval under exceptional circumstances in July 2013 under the trade name Imvanex for smallpox prevention, with the marketing authorization renewed in

April 2018 and expanded in July 2022 to include mpox and vaccinia virus disease for individuals aged 12 years and older (Imvanex, EMA).
The U.S. Food and Drug Administration (FDA) licensed the same vaccine as Jynneos in September 2019 for both smallpox and mpox prevention in adults aged 18 years and older, based on non-inferior immunogenicity data compared to second-generation vaccines and improved safety profiles (JYNNEOS, FDA).

Each 0.5 mL dose contains no less than 5 × 10^7 infectious units of live attenuated Modified Vaccinia Ankara-Bavarian Nordic virus, with trace residues of chicken protein, benzonase, gentamicin, and ciprofloxacin from the manufacturing process (Imvanex, EMA; JYNNEOS, FDA).

Conducting traditional efficacy trials against smallpox was unethical given disease eradication. Regulatory approval relied on demonstrated immunogenicity non-inferiority to second-generation vaccines (ACAM2000) through vaccinia virus neutralizing antibody responses, combined with animal challenge studies demonstrating 80 – 100 % survival in non-human primates against lethal monkeypox virus exposure (Bavarian Nordic), rather than direct human efficacy data against orthopoxviruses.

3.2 Vaccine Effectiveness (VE)[2]

3.2.1 Summary Findings

MVA-BN vaccination provides substantial protection against mpox, with meta-analytic effectiveness estimates of 76 % (95 % CI: 64 – 88 %) for single-dose and 82 % (95 % CI: 72 – 92 %) for two-dose regimens based on 32 studies enrolling over 110,000 participants during the 2022 clade IIb outbreak. Post-exposure prophylaxis demonstrates variable effectiveness (pooled estimate 20 %, 95 % CI: -24 – 65 %), though methodological limitations including immortal time bias constrain interpretation.

Antibody kinetics reveal rapid serological waning in vaccinia-naive individuals, with neutralizing titers returning to baseline within 5 – 7 months post-vaccination. Belgian cohort data show only 4 % of vaccinees retain detectable neutralizing antibodies at 8 months. Despite this decay, memory B-cell responses persist, and booster vaccination elicits strong anamnestic responses with nearly 90-fold rises in neutralizing titers. Mathematical modelling predicts 66.6 % effectiveness at 10 years for standard two-dose regimens, increasing to 77.6 % with extended dosing intervals.

Cross-clade protection is expected based on conserved T-cell epitopes (78 % CD8, 72 % CD4 epitope conservation), animal challenge studies, and regulatory licensing without clade restrictions.

Safety data from over 8,900 clinical trial participants and large-scale surveillance demonstrate predominantly mild-to-moderate injection site reactions. Myocarditis/pericarditis incidence is less than 1 per 100,000 doses, substantially lower than replicating vaccinia vaccines. MVA-BN safely vaccinates populations previously contraindicated for smallpox vaccination, including individuals with atopic dermatitis and HIV infection. Pediatric safety data support age de-escalation, with EMA approval for adolescents aged 12 – 17 years in September 2024.

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[2] Throughout this document, we primarily reference the meta-analytic pooled estimate (82 %, 95 % CI: 72 – 92 %) when discussing two-dose effectiveness, while noting that real-world effectiveness varies by population characteristics, follow-up duration, and local transmission dynamics.

3.2.2 General effectiveness and duration of protection

While MVA-BN regulatory approval relied on immunogenicity and animal studies, the 2022 global mpox outbreak subsequently generated extensive real-world effectiveness evidence in humans. Real-world observational studies conducted during the 2022 global mpox outbreak demonstrate that MVA-BN vaccination provides substantial protection against symptomatic infection, with meta-analytic estimates showing vaccine effectiveness of 76 % (95 % CI: 64 – 88 %) for single-dose regimens and 82 % (95 % CI: 72 – 92 %) for two-dose regimens. These pooled estimates derive from 32 studies enrolling over 110,000 participants, predominantly gay, bisexual and other men who have sex with men aged 18 – 49 years (Pischel et al., 2024). Pre-exposure prophylaxis studies report adjusted effectiveness ranging from 35 – 86 % for one dose and 66 – 90 % for two doses when assessed ≥ 14 days post-vaccination (Mason et al., 2024). Beyond preventing infection, MVA-BN attenuates clinical severity, including reduction of systemic symptoms and extragenital lesions (Mason et al., 2024). One California study reported reduced odds of hospitalization among vaccinated individuals (OR 0.27 for 1 dose, OR 0.20 for 2 doses), though this finding requires confirmation in other populations (Schildhauer et al., 2025).

Post-exposure prophylaxis demonstrates more variable effectiveness, with meta-analytic pooled estimates of 20 % (95 % CI: -24 – 65 %) (Pischel et al., 2024), though individual studies report adjusted estimates of 78 % and 89 % for single-dose administration (Mason et al., 2024). The pooled estimate has wide confidence intervals, limiting conclusions about PEP efficacy. The studies suffer from immortal time bias (participants must remain disease-free long enough to receive vaccination post-exposure), which overestimates vaccine effectiveness. However, sensitivity analyses suggest this overestimation is modest due to the short follow-up period (ITT vaccine effectiveness: 74.6 - 85.4 %).

International guidelines recommend administration within 4 days based on theoretical immune kinetics and pre-vaccination era smallpox observations, though no contemporary mpox studies demonstrate differential effectiveness by timing within a 14-day window. Operational constraints (diagnostic turnaround, contact tracing, scheduling) typically result in PEP administration 5 - 7 days post-exposure in outbreak settings. Overall, PEP effectiveness remains modest compared to pre-exposure vaccination, regardless of timing.

Protection correlates with vaccinia-binding antibody titers, with meta-regression demonstrating significant association between ELISA geometric mean titers (GMT) and vaccine effectiveness (Berry et al., 2024), though no validated correlate of protection has been established and MVA-BN induces lower neutralizing antibody responses compared to first-generation smallpox vaccines (Berry et al., 2024).

Antibody kinetics demonstrate rapid waning in vaccinia-naive populations, with neutralizing titers returning to baseline within 5 – 7 months post-second dose in individuals without prior smallpox vaccination (Oom et al., 2025), while remaining elevated in those with pre-existing vaccinia immunity. Peak neutralizing responses occur at 8 weeks post-vaccination with geometric mean Plaque Reduction Neutralization Test (50 %) (PRNT50) titers of 1:35 against mpox virus, declining below the 1:20 detection limit by 12 weeks in most vaccinia-naive recipients (Phipps et al., 2025). Longitudinal surveillance of 116 at-risk individuals demonstrated that two-thirds of baseline-negative vaccinees had undetectable or low antibody levels at one-year post-vaccination (van Leeuwen et al., 2024). Mpox-specific binding antibody responses show similar kinetics, with median ELISA titers declining from peaks of 112 (M1R) and 384 (B6R) at 3 weeks post-second dose to 38 and 82 respectively at 12 months (Collier et al., 2024).

Despite this serological decay, memory B cell responses remain detectable at one year in both naive and experienced vaccinees, and natural infection generates more durable neutralizing responses than vaccination (Oom et al., 2025). Cellular immune responses persist at

12 months post-vaccination (Matusali et al., 2024). Immunological memory persists beyond circulating antibody levels, demonstrated by strong anamnestic responses: healthcare workers vaccinated subcutaneously receiving boosters 5 years post-primary vaccination showed nearly 90-fold rises in neutralizing titers by day 14 (Priyamvada et al., 2025), while participants receiving boosters at 2 years achieved peak neutralizing GMTs of 80.7 (one-dose primary) and 125.3 (two-dose primary), exceeding primary vaccination peaks and remaining elevated at 6 months post-booster (Ilchmann et al., 2023). However, comparative analysis demonstrates vaccine-induced T cells show reduced cytotoxicity, lower migratory potential to infection sites, and weaker TCR clonal expansion compared to natural infection (Chen et al., 2025).

Long-term follow-up data from Belgium extending to 24 months post-vaccination demonstrate persistent differences between natural infection and vaccine-induced immunity. Among smallpox-naive individuals, MPXV infection maintains neutralizing antibodies up to 24 months, whereas only 4 % (95 % CI: 1 – 17 %) of MVA-BN vaccinees retained detectable neutralizing antibodies at 8 months, with even lower prevalence at later timepoints (Van Dijck et al., 2025). MVA-BN induced 0.39-fold lower (95 % CI: 0.25 – 0.62) Vaccinia Virus (VACV)-binding antibody concentrations and 0.60-fold lower (95 % CI: 0.46 – 0.79) MPXV-E8L antibody concentrations compared to natural infection at 8 months (Van Dijck et al., 2025). Intradermal vaccination further compromised immunogenicity, generating 0.26-fold lower (95 % CI: 0.17 – 0.39) VACV antibodies and 0.54-fold lower (95 % CI: 0.37 – 0.77) MPXV-E8L antibodies compared to subcutaneous administration (Van Dijck et al., 2025).

Modelling of vaccinia-binding antibody titers from 12 immunogenicity studies demonstrates biphasic decay with fast-phase half-life of 20.7 days (95 % CI: 18.2 - 24.0) and slow-phase half-life of 1,721 days (95 % CI: 971 – 6,459), approximately 4.7 years (Berry et al., 2024). Mathematical modelling predicts two-dose standard regimens maintain 71.8 % (95 % CI: 58 - 80.8) effectiveness at 2 years and 66.6 % (95 % CI: 48.8 - 78.2) at 10 years (Berry et al., 2024).

Extended dosing intervals augment both peak antibody responses and long-term protection: delaying the second dose from 28 days to 730 days increases peak antibody titers 3.2-fold (95 % CI: 2.6 - 3.8) and produces 14.1-fold (95 % CI: 10.9 - 18.3) higher titers at one year post-boost, with predicted 10-year effectiveness of 77.6 % (95 % CI: 65.7 - 85.4) (Berry et al., 2024). The proportion of long-lived antibodies increases significantly with extended dose spacing, likely reflecting enhanced germinal center maturation and memory B cell differentiation. The absence of standardized correlates of protection and limited data on cellular immunity constrain predictions about long-term vaccine durability, particularly given that correlates identified shortly after vaccination may not predict effectiveness as immunity wanes.

Recent Australian cohort data spanning a median 22-month interval between second dose and symptom onset demonstrate 89 % reduced hospitalization risk (RR 0.11, 95 % CI: 0.03 – 0.43) and 28 % reduction in systemic symptom risk (RR 0.72, 95 % CI: 0.64 – 0.80) among fully vaccinated individuals (Latham et al., 2025), suggesting clinical protection persists beyond antibody waning. The discordance between serological waning and maintained clinical effectiveness occurs despite laboratory evidence showing antibody titers decline within 5 – 7 months of vaccination, raising the possibility of non-antibody correlates including cellular immunity and mucosal responses.

These findings suggest booster strategies merit further study for high-risk groups, particularly men who have sex with men, healthcare workers, and intradermal vaccine recipients. Rapid antibody decay by 8 - 12 months suggests booster strategies should be considered, though optimal timing remains undefined and questions persist about whether boosters restore strong responses and how durability compares to primary vaccination.

3.2.3 Cross-clade protection

MVA-BN vaccine effectiveness against clade IIb mpox is well-established from real-world data across multiple continents, with two-dose pre-exposure prophylaxis demonstrating protection in outbreak settings (Berry et al., 2024; Mason et al., 2024; Pischel et al., 2024).
Real-world effectiveness data against clade I remains limited as of early 2025. The SMART clinical trial in DRC is assessing post-exposure MVA-BN effectiveness following the September 2024 launch (Kumar et al., 2025). However, protection against clade I is expected based on immunologic cross-reactivity within the orthopoxvirus genus, where vaccines demonstrate cross-protection against multiple species.

The earliest studies of individuals vaccinated with first-generation smallpox identified vaccine effectiveness estimates against mpox infection during the 1980s of 82 – 85 % (Fine et al., 1988; Ježek et al., 1987; Jezek et al., 1988). A more recent European study identified a slightly lower pooled first-generation smallpox VE of 70 % (95 % CI: 23 - 89) during the 2022 Clade IIb epidemic, indicating that historic first-generation smallpox vaccination induced protection, albeit with indications of waning immunity over time (Colombe et al., 2024). Cessation of routine smallpox vaccination coincided with increased mpox emergence in endemic African countries (Rimoin et al., 2010). Contemporary systematic reviews confirm two-dose MVA-BN effectiveness of 82 % (95 % CI: 72 – 92 %) against clade IIb (Pischel et al., 2024), supporting expectations for pan-orthopoxvirus protection. Analysis of experimentally defined poxvirus epitopes shows that 78 % of CD8 epitopes and 72 % of CD4 epitopes are conserved between vaccinia virus and clade IIb MpoxV (Chen et al., 2025).

Animal challenge studies confirm cross-protection. MVA-BN administered subcutaneously or intradermally provided significant protection against high-dose intravenous challenge with clade IIb MpoxV in macaques (Herate et al., 2025; Hillus et al., 2025). Non-human primates vaccinated with recombinant MVA survived lethal MPXV challenge up to 3 years post-vaccination despite low neutralizing antibody levels (Phipps et al., 2025), also suggesting that correlates of protection involve memory B-cells and cellular immune responses rather than neutralizing antibodies alone.

Regulatory authorities license MVA-BN without clade-specific restrictions, reflecting this pan-orthopoxvirus protection. Both MVA-BN and LC16m8 hold approval for mpox prevention regardless of viral clade (Grabenstein & Hacker, 2024; Imvanex, EMA). ECDC assessments state "the same vaccine is expected to work for both clades" based on conserved T-cell epitopes and animal challenge data (Grabenstein & Hacker, 2024).

3.3 MVA-BN Vaccine Safety

MVA-BN demonstrates a favorable safety profile across diverse populations, though reactogenicity varies by administration route and recipient characteristics. Pooled meta-analysis of clinical trials involving 8,988 participants aged 18 - 80 years documented predominantly mild-to-moderate injection site reactions resolving within seven days without intervention (Pang et al., 2024). Subcutaneous administration demonstrates lower local adverse event rates (53 %, 95 % CI: 33 – 73 %) compared with intradermal injection (75 %, 95 % CI: 31 – 118 %), with similar patterns for systemic reactions (23 % vs 30 %, respectively) (Pang et al., 2024). Canadian CANVAS prospective active surveillance of 1,173 vaccinated participants found mild-to-moderate injection site pain in 60 %, health events preventing normal activities or requiring medical assessment in 3.3 % vaccinated versus 7.1 % controls ($p<0.010$), zero hospitalizations within 30 days, and no cases of myocarditis, severe neurological disease, or skin disease (Muller et al., 2024). Complementary US surveillance confirmed comparable safety across diverse healthcare settings (Back et al., 2024). Large-scale German multicenter surveillance of 6,459 participants reported adverse reactions in

0.35 % after first dose and 0.14 % after second dose, with predominantly mild local and systemic reactions (Hillus et al., 2025). These general population data enabled evaluation of historically high-risk groups previously contraindicated for replicating vaccinia vaccines.

Individuals with atopic dermatitis experienced higher injection site erythema (61.2 % vs 49.3 %) and swelling (52.2 % vs 40.8 %) compared with healthy controls, alongside increased headache frequency (33.1 % vs 24.8 %) (Imvanex, EMA), but no eczema vaccinatum or serious cutaneous dissemination occurred (Greenberg et al., 2015), contrasting with replicating vaccinia vaccines where eczema vaccinatum represented a life-threatening complication necessitating absolute contraindication for patients with atopic dermatitis (Vora et al., 2008). MVA-BN's non-replicating platform enabled safe vaccination of 350 atopic dermatitis patients in clinical trials without serious cutaneous adverse events (Greenberg et al., 2015), with subsequent global pharmacovigilance and regulatory assessments confirming this favourable safety profile (*Mpox*, n.d.-b).

Cardiovascular safety surveillance establishes reassuring myocarditis/pericarditis signals substantially lower than replicating vaccinia vaccines. Global Bavarian Nordic pharmacovigilance database encompassing 9,585 adverse events reports myocarditis/pericarditis incidence less than 1 per 100,000 doses (Weidenthaler et al., 2024), contrasting with ACAM2000's 20.06 per 100,000 rate (Decker et al., 2021). Prospective European surveillance of 6,459 participants documented zero myocarditis or pericarditis cases, with one self-resolving intermittent arrhythmia (Decker et al., 2021). Post-authorization Vaccine Safety Datalink analysis of 53,583 adults receiving dose 1 and 38,206 receiving dose 2 found no statistically significant elevated standardized incidence ratios for ten prespecified adverse events of special interest, including cardiovascular outcomes (Duffy et al., 2024).

Immunocompromised populations demonstrate consistent vaccine safety without increased serious adverse events. Pooled effectiveness studies included 15,867 HIV-positive individuals across diverse clinical settings (Pischel et al., 2024). In Canadian surveillance, HIV-positive participants (8.4 % of cohort) exhibited less frequent local reactions (48 % vs 61 %, p=0.021) but more health events requiring medical assessment (7.1 % vs 3.1 %, p=0.04), primarily non-specific systemic symptoms, headache, and gastrointestinal complaints, likely reflecting baseline health complexity and older age (median 50 - 64 vs 30 - 39 years) rather than vaccine toxicity (Muller et al., 2024).The lower local reactogenicity likely reflects attenuated immune responses in immunocompromised individuals, while increased healthcare-seeking events relate to baseline health complexity rather than vaccine-specific toxicity. Limited data from transplant recipients and those receiving immunosuppressive therapy show no safety signals, though systematic surveillance remains sparse.

Paediatric safety data support cautious age de-escalation beyond original adult licensing. Among children under 12 years, UK post-exposure prophylaxis documented 87 recipients (median age 5 years) with no serious adverse events or mpox development, local reactions in 40 %, and systemic symptoms in 24 % (Ladhani et al., 2023). Phase 2/3 African trial data from 227 children aged 2 - 11 years demonstrated comparable safety to adults with 2.5-fold higher immune responses (Bavarian Nordic). For adolescents aged 12 - 17 years, WHO and EMA approved MVA-BN in September 2024 based on accumulated safety evidence.

Pregnancy and lactation data remain limited. Fewer than 300 documented pregnancy exposures show no adverse outcomes or teratogenic signals, though systematic surveillance is lacking (Imvanex, EMA). Animal reproductive toxicology studies demonstrate no impaired fertility or fetal harm. The absence of concerning signals contrasts with replicating vaccinia vaccines' documented foetal risks, but insufficient human data preclude definitive safety conclusions for routine pre-exposure prophylaxis during pregnancy (Imvanex, EMA).

3.4 Administration

3.4.1 Subcutaneous Administration

Subcutaneous administration of MVA-BN vaccine at 0.5 ml per dose represents the standard, EMA-approved route with the most extensive safety and immunogenicity data (Imvanex, EMA).

3.4.2 Intradermal Administration

Intradermal administration at 0.1 ml per dose (one-fifth of the standard subcutaneous dose) serves primarily as a dose-sparing strategy during vaccine shortage situations, enabling five-fold dose multiplication from a single vial. Emergency use authorizations issued by the US FDA and EMA Emergency Task Force (EMA's Emergency Task Force) permitted fractional dosing based on immunologic principles that the dermis contains higher concentrations of immune-stimulating dendritic cells and Langerhans cells compared to subcutaneous tissue. A randomized Phase 2 trial (NCT05512949) demonstrated non-inferior antibody levels at day 43 (two weeks post-second dose) comparing intradermal 0.1 ml (2×10^7 $TCID_{50}$) to subcutaneous 0.5 ml (1×10^8 $TCID_{50}$) dosing, though intradermal antibodies declined more rapidly by day 57 (Frey et al., 2025).

Intradermal administration requires training in proper technique using 1 ml syringes with 25 - 27-gauge needles inserted 2 - 3 mm into dermis at 5 - 15° angle to produce the characteristic tense blanched wheal (CHMP, n.d.; Payne et al., 2025).
Keloid history contraindicates (relative) intradermal but not subcutaneous vaccination. Informed discussion should address route-specific scarring risks.

3.4.3 Preferred route

With restoration of adequate vaccine supply by 2024 - 2025, most international authorities now prefer subcutaneous administration, reserving intradermal dosing as a contingency strategy for future outbreak scenarios with supply constraints (EU4Health; CDC).

MVA-BN's non-replicating nature makes it safe for immunosuppressed individuals regardless of route (Grabenstein & Hacker, 2024); however, severely immunosuppressed persons preferably receive subcutaneous administration due to potential reduced immunogenicity with intradermal dosing.

EMA approved subcutaneous administration for adolescents aged 12 - 17 years in September 2024. International authorities recommend subcutaneous administration for pregnant individuals when vaccination is warranted, as intradermal immunogenicity data in pregnancy are absent.

3.5 Contraindications

The EMA product information establishes a single absolute contraindication for MVA-BN: hypersensitivity to the active substance, excipients, or trace residues (chicken protein, benzonase, gentamicin, ciprofloxacin). The product information lists precautions rather than contraindications: immunization should be postponed in acute severe febrile illness or infection, though minor illness permits vaccination (Imvanex, EMA).

3.6 Coadministration with other vaccines

Controlled trial data on co-administering MVA-BN with HPV, herpes zoster, pneumococcal, or influenza vaccines are unavailable (Imvanex, EMA).

Standard immunization practice permits simultaneous administration when no contraindications exist.

3.7 Populations with additional considerations

3.7.1 People living with HIV

MVA-BN demonstrates reduced single-dose effectiveness in people living with HIV (34.9 %, 95 % CI: -72.8 to 79.0) compared to HIV-negative persons (84.1 %, 95 % CI: 42.0 - 100) (Hillus et al., 2025). Immunocompromised populations achieve 70.2 % protection after two doses versus 87.8 % in immunocompetent individuals (Dalton et al., 2025). MVA-BN immunogenicity in virologically suppressed HIV-positive participants with CD4 > 100 cells/µL shows seroconversion rates of 92.7 % by day 42 following two-dose regimens by ELISA (Imvanex, EMA), with no safety concerns identified given the non-replicating vaccine platform.

International consensus emphasizes two-dose completion for immunocompromised populations, with France implementing three-dose primary series and UK recommending booster intervals of two years for severely immunosuppressed persons versus ten years for immunocompetent populations (The Green Book, UK).

3.7.2 Pregnancy

Human vaccination safety data remain limited to fewer than 300 pregnancy exposures (Imvanex, EMA; The Green Book, UK). Animal developmental toxicity studies in rats and rabbits demonstrate no fetal harm (Imvanex, EMA). The vaccine's non-replicating platform cannot be reproduced in human cells, providing theoretical safety reassurance (Nachega et al., 2024).

WHO, UKHSA, and CDC ACIP converge on shared logic: theoretical vaccination risk must be weighed against documented maternal disease severity and fetal risks including demise, preterm delivery, and vertical transmission (Rao et al., 2025; GACVS). CDC ACIP published no routine pregnancy recommendation in June 2025, noting insufficient human data while stating vaccination should not be withheld when exposure risk is significant (Rao et al., 2025).

Recommendations should adopt precautionary language but explicitly permit vaccination when benefits outweigh risks, aligning with international consensus on individual risk-benefit assessment.

3.7.3 Pediatric considerations

Infants Under Age Two

Direct mpox vaccination data in infants remains limited. MVA-BN platform safety in young children derives from the MVA-BN-Filo Ebola vaccine. The MVA-BN-Filo Ebola vaccine demonstrated safety in > 800 children aged 1 - 17 years in Africa with a profile comparable to adults, including infants as young as 4 months without vaccine-related serious adverse events (E. M. L. Choi et al., 2023). Since adverse events from MVA vaccines primarily relate to the vector rather than the inserted antigens, these data provide relevant safety information for MVA-BN mpox vaccination in young children.

For mpox vaccination, parallel trials began June 2025 enrolling 344 infants aged 4 - 24 months (NCT06844487) in DRC, comparing full dose versus half-dose regimens (CEPI). WHO GACVS emphasized standardized safety monitoring given limited data for this age group (GACVS).

Children Ages 2 - 11 Years

Pediatric immunogenicity trials (ages 2 - 11 years) show non-inferior immune responses to adults with acceptable safety profiles (Bavarian Nordic). EMA approval for this age group is anticipated in 2026.

Post-exposure prophylaxis with single-dose MVA-BN in 87 English children (median age 5 years among 45 responding to questionnaires, IQR 5 - 9) showed no serious adverse events (Ladhani et al., 2023).

Adolescents Ages 12 - 17 Years

EMA extended Imvanex indication to adolescents aged 12 - 17 years in September 2024, adopted by the European Commission September 19, 2024. Approval followed Phase 2 trial data comparing 315 adolescents with 211 adults (NCT05740982), demonstrating GMT ratio 1.60 (95 % CI: 1.32 - 1.95) with comparable adverse event profiles between age groups (Healy et al., 2025).

UKHSA recommends 0.5 mL subcutaneous or intramuscular dosing for all children under 18 (The Green Book, GOV.UK)

3.7.4 Pre-deployment and Travel Vaccination Timing

Travelers to mpox-endemic areas should initiate vaccination at least 6 weeks before departure to complete the two-dose series and achieve peak immunity. The standard regimen requires doses administered 28 days apart (minimum 4 weeks), with optimal antibody responses achieved approximately 14 days after the second dose. This timing ensures travellers receive dose 1 at departure minus 6 weeks, dose 2 at departure minus 2 weeks, and reach presumed optimal protection at time of travel.

Travelers unable to complete the series before departure should receive at least one dose, as partial immunity provides meaningful risk reduction during exposure. Single-dose recipients departing before completing the series achieve partial protection (effectiveness 36 – 75 % versus 66 – 89 % for two doses) and should complete the second dose upon return.

4 Modelling

No Belgium-specific modelling addresses vaccine efficacy, coverage thresholds, or cost-effectiveness. Limited data is available in literature.
Modelling of the 2022 clade IIb outbreak in European MSM demonstrated that infection-derived immunity contributed minimally to outbreak control (Hvid et al., 2025). The model, which incorporated survey data on sexual behaviour and the heterogeneous nature of sexual contact networks, revealed a marked decrease in serial interval throughout the epidemic that reflected substantial increases in self-isolation behaviour among infected persons. This behavioural adaptation proved sufficient to explain early epidemic control independent of immunity accumulation. The analysis confirmed that while adaptive behaviours curtailed the initial outbreak, the European MSM population remains protected primarily through vaccine-induced immunity rather than natural infection, underscoring vaccination's continued importance despite reduced transmission intensity.

Modeling studies estimate minimum vaccine coverage thresholds of 14.5 - 19.5 % would be required to prevent epidemic growth in clade I-affected countries under scenarios with high sexual transmission (Jin et al., 2025). These estimates derive from next-generation matrix models calibrated to clade Ib outbreak data from South Kivu, DRC, though countries with high community contact patterns may require coverage exceeding 30 % to achieve outbreak control

(Jin et al., 2025). However, these results are not directly generalizable to the Belgian context as transmission dynamics differ.

Economic modeling from England demonstrates mpox vaccination for high-risk GBMSM populations is cost-saving rather than merely cost-effective. Zhang et al (Zhang et al., 2025) evaluated vaccination strategies over 10 years using transmission models calibrated to 2022 outbreak data. Assuming vaccine effectiveness of 78 %/89 % for one/two doses, protection durations of 5/10 years, and costs of £160 per dose, all vaccination strategies tested (pre-emptive vaccination at 13 - 135 doses/day, reactive vaccination at 81 - 204 doses/day, and combined pre-emptive plus reactive strategies) reduced outbreak costs and gained Quality-Adjusted Life Years (QALYs) compared to no vaccination. Combined continuous pre-emptive vaccination (54 doses daily) with reactive outbreak vaccination (81 doses daily) saved £8.8 million and gained 108.6 QALYs over 10 years. Vaccination remained cost-effective if vaccine costs remained below £330 per dose. The model used Global Burden of Disease disability weights for generic acute infections rather than mpox-specific QALY estimates, potentially underestimating psychosocial sequelae including stigma and sexual dysfunction. Substantial uncertainties limit applicability to Belgium. Assumed vaccine costs likely differ from Belgian pricing. Baseline epidemiological projections (306 cases in 2024 increasing to 3,332 in 2033 without vaccination) may not reflect Belgian transmission dynamics.

No analyses address clade Ib cost-effectiveness.

5 International recommendations

International authorities converge on two-dose MVA-BN vaccination targeting gay, bisexual, and other men who have sex with men with specific risk factors. WHO, CDC, ECDC, UK, Canada, France, Germany, and Netherlands identify MSM with recent sexually transmitted infections, multiple partners, HIV PrEP use, or sex at commercial venues as eligible populations (Pischel et al., 2024). Sex workers of all genders receive explicit inclusion in pre-exposure prophylaxis programs (Rapid Scientific Advice on Public Health Measures for Mpox (2024 - 2025)). Healthcare worker vaccination targets laboratory personnel handling Orthopoxvirus specimens, infectious disease and dermatology/sexual health clinic staff managing confirmed or suspected cases, and outbreak response teams with potential exposure, rather than routine occupational vaccination (Rapid Scientific Advice on Public Health Measures for Mpox (2024 - 2025)).

International consensus establishes within four days of exposure as the optimal post-exposure prophylaxis window for disease prevention, yet WHO systematic reviews document only 20 % PEP effectiveness (95 % CI: -24 % to 65 %) across seven studies (Pischel et al., 2024), substantially lower than 82 % two-dose pre-exposure vaccination. WHO guidance (WHO) recommends PEP for confirmed case contacts, sexual partners within preceding two weeks, household contacts, and healthcare workers with documented exposure. CDC and ECDC guidelines recommend PEP up to 14 days post-exposure, with case-by-case consideration beyond 14 days for severely immunocompromised persons based on individual risk-benefit assessment (CDC; Rapid Scientific Advice on Public Health Measures for Mpox (2024 - 2025)). UK UKHSA (The Green Book, GOV.UK) extends to 14 days for immunosuppressed, pregnant, or children under five for disease modification. France’s *Haute Autorité de Santé* (HAS) specifies maximum 14 days post-exposure. WHO and CDC introduced PEP++ strategies targeting presumed contacts without documented exposure when case numbers justify expanded reach. Standard PEP targets documented contacts of confirmed cases (household contacts, sexual partners, healthcare workers with known exposure). PEP++ extends vaccination to presumed contacts without documented exposure, meaning persons with specific risk factors who likely experienced recent exposure even without verifiable contact tracing.

International mpox vaccination strategies for travellers reveal marked disparities in accessibility and pragmatism. France adopted the most explicit approach targeting visitors to family and relatives, recommending vaccination for persons visiting family in clade I transmission areas, alongside humanitarian workers and immunocompromised travellers (*Mesures de Prévention Pour Les Voyageurs Vis-à-Vis Du Mpox*, n.d.). This position aligns with broader European guidance suggesting vaccination for travellers "visiting families or planning close contact with people in areas with active MPXV clade I circulation" (*Rapid Scientific Advice on Public Health Measures for Mpox (2024 - 2025)*, n.d.-a). In contrast, Germany's *Ständige Impfkommission* (Standing Committee on Vaccination) issued no travel vaccination recommendation (Robert Koch Institute), while the UK restricted pre-travel vaccination to specialist healthcare and humanitarian workers responding to active outbreaks (National Travel Health Network and Centre). Canada's May 2025 framework pragmatically recommends vaccination for travellers to clade I transmission areas who anticipate prolonged close contact or sexual contact with residents, delivered through provincial programs using self-attestation without specialist gatekeeping (Canada.Ca). In contrast, most European countries including Germany and the Netherlands do not currently offer mpox vaccination specifically for travellers, instead focusing vaccination programs exclusively on domestic high-risk populations, primarily men who have sex with men (RIVM; Rapid Scientific Advice).

CDC recommends completing the two-dose series with first dose at least six weeks pre-departure (CDC), creating substantial logistical barriers for travellers with shorter planning horizons, particularly problematic for VFR travellers who often have limited advance notice for family emergencies or cultural obligations.

6 Operational considerations

6.1 Pre- and Post Vaccination implementation:

Based on epidemiological transmission dynamics, the highest risk group in Belgium includes people with multiple changing sexual partners, in particular among sexual networks of gay or bisexual men having sex with men (GBMSM). Therefore, Mpox vaccination should be integrated into routine sexual health services at HIV Reference Centers rather than implemented as a separate campaign. The vaccine can be offered opportunistically during regular clinical visits (PrEP consultations, HIV follow-up appointments, sexually transmitted infection (STI) screening) over the coming months and years. This approach leverages existing trust-based relationships between clinicians and patients, normalizes Mpox vaccination within sexual health care, and allows gradual uptake without requiring additional infrastructure or dedicated vaccination sessions. HIV Reference Centers already provide services to the populations at highest risk (PrEP users, people living with HIV, individuals with multiple STI episodes) and maintain documentation systems that enable aggregated surveillance without compromising individual privacy. To facilitate vaccination uptake among sex workers, collaboration with community-based organizations (CBOs) dedicated to sex worker communities could support outreach and service accessibility.

6.2 Travel-related vaccination

Travel clinics affiliated with HIV Reference Centers can provide mpox vaccination to travelers when indicated. Given Belgium's historical ties with endemic regions and occasional travel to outbreak-affected areas, clinicians should assess individual risk based on destination, planned activities, and potential exposure scenarios. This follows from the fact that this remains a niche indication requiring case-by-case evaluation rather than broad recommendations for all travelers to affected regions.

6.3 Monitoring and evaluation

HIV reference centers can document vaccination status and report anonymized aggregate data (number of doses administered, indication for administration (pre- vs post-exposure), age group distribution, gender, risk group) to provide overview of population immunity and inform public health strategy, without requiring individuals to disclose personal sexual orientation or detailed sexual behaviour data as a condition for vaccination access to other parties than the health care provider. The HIV reference centres could provide aggregated data for real-world effectiveness and program evaluation. In Flanders, vaccinations administered are already registered in Vaccinet; similar centralized documentation exists in Brussels and Wallonia.

7 Future Research Priorities for Mpox Vaccination

Four critical evidence gaps constrain policy development. No prospective clade I effectiveness data exist, requiring empirical validation of assumed cross-protection. The SMART trial (NCT05745987) in DRC, Uganda, and Nigeria will provide the first randomized controlled evidence for post-exposure prophylaxis in household contacts, with results anticipated to inform clade I outbreak strategies. Immunocompromised populations show substantially reduced protection, necessitating stratified studies by CD4 count and optimal dosing strategies. Durability demonstrates paradoxical dissociation between rapid antibody waning (5 - 7 months) and sustained clinical protection extending beyond 24 months, highlighting the absence of validated correlates of protection.

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VI COMPOSITION OF THE WORKING GROUP

The composition of the Committee and that of the Board as well as the list of experts appointed by Royal Decree are available on the following website: About us.

All experts joined the working group ***in a private capacity***. Their general declarations of interests as well as those of the members of the Committee and the Board can be viewed on the SHC website (site: conflicts of interest).

The following experts were involved in drawing up and endorsing this advisory report. The working group was chaired by **Steven CALLENS**; the scientific secretaries were Laura KOSTOV and Veerle MERTENS.

BLOT Koen	Epidemiology, infectious diseases	Sciensano
CALLENS Steven	Internal Medicine, infectious disease medicine, emerging communicable diseases, travel medicine, vaccinology, tuberculosis, AIDS-HIV, ebola, COVID-19	*UGent, UZ Gent*
DE SCHEERDER Marie-Angélique	Internal medicine, infectious disease medicine, travel medicine, AIDS-HIV, anti-bacterial agents	*UGent, UZ Gent*
LIBOIS Agnès	Infectious diseases	*CHU Saint-Pierre*
LIESENBORGH Laurens	Infectiology, humanitarian specialists	ITG-ITM-IMT
VAN DIJCK Christophe	Internal medicine, clinical emerging infectious diseases	ITG-ITM-IMT
VAN LAETHEM Yves	Infectiology, vaccinology and travel medicine	*exCHU Saint-Pierre*, ULB

The following experts or administrations were heard but did not take part in endorsing the advisory report.

DRAGUEZ Bernard	Health Inspection Advisor	FPS Health, RMG
ROLIN Florence	General medecine	Vivalis
THEETEN Heidi	Vaccinology	VAZG

The standing working group NITAG has endorsed the advisory report. The standing working group NITAG was co-chaired by **Steven CALLENS** and **David TUERLINCKX**; the scientific secretaries were Laura KOSTOV, Veerle MERTENS and Michael PEETERS. This document was approved at the NITAG meeting held on January 29, 2026. The following members were present at the meeting:

ALDERS Nele	Pediatrics, infectiology, travel and tropical medicine	ITG
BEUTELS Philippe	Social sciences, health care economics and organizations, infectious disease medicine	*UAntwerpen*, CHERMID, SIMID
BLUMENTAL Sophie	Pediatrics, infectious disease medicine, vaccinology, primary immunodeficiency diseases,	ULB, CHIREC

	pneumococcal infections, tuberculosis	
BOIY Tine	Pediatrics, rare diseases, congenital hereditary and neonatal diseases and abnormalities, down syndrome.	*UAntwerpen*, UZA
CALLENS Steven	Internal medicine, infectious disease medicine, emerging communicable diseases, travel medicine, vaccinology, tuberculosis, AIDS-HIV, ebola, COVID-19	*UGent, UZ Gent*
CARRILLO SANTISTEVE Paloma	General practice, infectious disease medicine, vaccinology, preventive medicine, public health	ONE
CHATZIS Olga	Pediatrics, infectious disease medicine, congenital hereditary and neonatal diseases and abnormalities, vaccinology	*UCLouvain, Cliniques universitaires Saint-Luc*
CHRISTIAENS Thierry	Pharmacology.	CBIP/BCFI, *UGent*
CORNELISSEN Laura	Obstetrics, gynecology, epidemiology, infectious disease medicine, maternal health, public health	Sciensano
DE COSTER Ilse	Head of the Ambulatory Trial Unit	*UAntwerpen*
DE SCHEERDER Marie Angélique	Internal medicine, infectious disease medicine, travel medicine, AIDS-HIV, anti-bacterial agents	*UGent, UZ Gent*
DE SCHRYVER Antoon	Occupational and environmental medicine	*UAntwerpen*
DESMAELE Sara	Pharmacology	CBIP/BCFI
DESMET Stéfanie	Clinical microbiology, epidemiology	*UZ Leuven*, NRC for Pneumococci
DOGNE Jean Michel	Pharmacy and pharmacovigilance	*UNamur*, AFMPS, EMA
FRERE Julie	Pediatrics and infectiology	*CHU Liège*
MAERTENS Kirsten	Vaccinology and maternal immunization	*UAntwerpen*
MANIEWSKI-KELNER Ula	Infectiology and travel medicine	ITG-IMT-ITM
SMEESTERS Pierre	Pediatrics, infectiology, vaccinology	HUDERF
SOENTJENS Patrick	Travel medicine, vaccinology, zoonotic diseases, HIV	ITG-IMT-ITM, Defense
SWENNEN Béatrice	Epidemiology and vaccinology	ULB
TUERLINCKX David	Pediatrics and vaccinology	*CHU UCL Namur*

VAN DAMME Pierre	Epidemiology, vaccinology, infectiology, public health	*UAntwerpen*
VAN LAETHEM Yves	Infectiology, vaccinology and travel medicine	*ex-CHU Saint-Pierre*, ULB
VANDEN DRIESSCHE Koen	Pediatrics, infectiology, oncology	UZA
WAETERLOOS Geneviève	Quality of vaccines and blood products	Sciensano

The following experts were heard but did not take part in endorsing the advisory report:

DAEMS Joël	Directorate Drugs	RIZIV-INAMI
SABBE Martine	Vaccinovigilance and safety of vaccines	AFMPS-FAGG
THEETEN Heidi	Vaccinology	VAZG
TEUGHELS Stefan	Medical Director Domus Medica general medicine, public health, EBM	Domus Medica

About the Superior Health Council (SHC)

The Superior Health Council is a federal advisory body. Its secretariat is provided by the Federal Public Service Health, Food Chain Safety and Environment. It was founded in 1849 and provides scientific advisory reports on public health issues to the Ministers of Public Health and the Environment, their administration, and a few agencies. These advisory reports are drawn up on request or on the SHC's own initiative. The SHC aims at giving guidance to political decision-makers on public health matters. It does this on the basis of the most recent scientific knowledge.

Apart from its 25-member internal secretariat, the Council draws upon a vast network of over 500 experts (university professors, staff members of scientific institutions, stakeholders in the field, etc.), 300 of whom are appointed experts of the Council by Royal Decree. These experts meet in multidisciplinary working groups in order to write the advisory reports.

As an official body, the Superior Health Council takes the view that it is of key importance to guarantee that the scientific advisory reports it issues are neutral and impartial. In order to do so, it has provided itself with a structure, rules and procedures with which these requirements can be met efficiently at each stage of the coming into being of the advisory reports. The key stages in the latter process are: 1) the preliminary analysis of the request, 2) the appointing of the experts within the working groups, 3) the implementation of the procedures for managing potential conflicts of interest (based on the declaration of interest, the analysis of possible conflicts of interest, and a Committee on Professional Conduct) as well as the final endorsement of the advisory reports by the Board (ultimate decision-making body of the SHC, which consists of 30 members from the pool of appointed experts). This coherent set of procedures aims at allowing the SHC to issue advisory reports that are based on the highest level of scientific expertise available whilst maintaining all possible impartiality.

Once they have been endorsed by the Board, the advisory reports are sent to those who requested them as well as to the Minister of Public Health and are subsequently published on the SHC website (www.hgr-css.be). Some of them are also communicated to the press and to specific target groups (healthcare professionals, universities, politicians, consumer organisations, etc.).

In order to receive notification about the activities and publications of the SHC, please contact: info.hgr-css@health.belgium.be.

Notes

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