UK Health Security Agency

Recommendations for the use of pre- and post-exposure vaccination during a monkeypox incident

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Contents

Background

Monkeypox is a rare disease that is caused by infection with monkeypox virus which is a DNA virus. With the eradication of smallpox in 1980 and subsequent cessation of smallpox vaccination, it has emerged as the most important, dominant orthopoxvirus. Monkeypox occurs sporadically in central and western parts of Africa's tropical rainforest.

As monkeypox is related to the virus causing smallpox, vaccines designed for smallpox will likely provide a degree of cross-protection. Previous data from Africa suggests that previous vaccines against smallpox may be up to 85% effective in preventing monkeypox infection. In recognition of this protection, there is extant policy in the Green Book (Immunisation Against Infectious Diseases) (1) which recommends that:

> "Workers in laboratories where pox viruses (such as monkeypox or genetically modified vaccinia) are handled, and others whose work involves an identifiable risk of exposure to pox virus, should be advised of the possible risk and smallpox vaccination should be considered. Detailed guidance for laboratory staff has been prepared (Advisory Committee on Dangerous Pathogens and the Advisory Committee on Genetic Modification, 1990)".

Historically, first and second generation live (replication competent) smallpox vaccines have been used for population-level and targeted occupational health-related immunisation programmes in the UK. The infant programme ceased in 1971, with variable uptake in the preceding decades. Apart from healthcare workers vaccinated in 2003 to 2004 and more recently, vaccinated individuals who will be older, and should have a distinctive scar (which normally looks like a circular 5p size dent in the left upper arm). The first and second generation live smallpox vaccines are reactogenic and associated with risks of other serious adverse events. The newer third generation smallpox vaccines have a much-improved side effect profile compared with first and second generation smallpox vaccines and do not result in a scar unlike the earlier vaccines.

The modified vaccinia Ankara (MVA-BN) (Imvanex) vaccine, a third generation smallpox vaccine has been licensed by European Medicines Agency (2) in 2013 for the prevention of smallpox and in 2022 for the prevention of monkeypox. In September 2019, the Food and Drug Administration (FDA) in the US approved MVA-BN (JYNNEOS) for the prevention of monkeypox as well as smallpox.

This document summarises the available data on MVA-BN (Imvanex/ JYNNEOS) including from previous experience of use of this vaccine in contacts of monkeypox cases in the UK. It details the current advice of an expert working group (see Appendix 1 for details) and the UK Joint Committee on Vaccination and Immunisation (JCVI) on the use of this vaccine for pre- and post-exposure use in England.

MVA-BN (Imvanex / Jynneos)

MVA-BN is a third generation live (replication defective) modified vaccinia Ankara vaccine, manufactured by Bavarian Nordic (3). The virus used in the vaccine is attenuated through multiple passages in chicken embryo fibroblast cells, leading to a substantial loss of its genome. Many of the known immune evasion and virulence factors are not encoded. It demonstrates very limited replication capability and low neuropathogenicity in human and animal studies, while retaining immunogenic properties, including demonstrable protective immune responses against a variety of orthopoxviruses (4).

MVA-BN is approved by the Medicines and Healthcare products Regulatory Agency (MHRA) for the prevention of smallpox and the European Medical Agency (Imvanex) for the prevention of smallpox and monkeypox, and is approved by the FDA (JYNNEOS) for prevention of small pox and monkeypox in the US (5). Whilst the vaccine has recently been authorised for protection against monkeypox in Europe, for the current UK stock, this indication is still considered 'off-label'.

On 9 August 2022, the US FDA issued an Emergency Use Authorisation (EUA) for the emergency use of JYNNEOS for the active immunisation by intradermal injection (0.1ml) for the prevention of monkeypox disease amongst adults aged 18 years and above, at high risk of infection. In the context of the national public health emergency declared in the US, this alternative regimen was approved to increase the number of available JYNNEOS doses by up to 5-fold. JCVI has also endorsed this approach to maximise the number of doses that can be administered without compromising immunity. On 19 August 2022, the European Medicines Agency Emergency Task Force released a statement concluding that intradermal use of MVA-BN vaccine was acceptable in view of the outbreak situation and significant vaccine shortage.

Efficacy

While MVA-BN efficacy studies were aimed at understanding its protective efficacy against smallpox, many of the licensing studies have been conducted using challenge with monkeypox virus.

In a macaque model, 2 doses of MVA-BN have been shown to induce 100% protection against a lethal challenge of aerosolised monkeypox (6) A separate study in cynomolgus macaques demonstrated no significant difference between the levels of neutralising antibody in animals vaccinated with ACAM2000 (a second-generation smallpox vaccine) and those vaccinated with 2 doses of MVA-BN (7). Protection after a single dose of MVA-BN was also studied in a macaque challenge model: when compared to Dryvax (a first-generation live smallpox vaccine) MVA-BN produced earlier detectable antibody (on day 7) and provided complete protection against fatal monkeypox (4/4) at 4 days with only one clinical case in 16 animals challenged between 6 and 30 days after the first dose.

Preclinical studies and phase I/II clinical trials of MVA-BN have suggested that 2 doses of subcutaneous vaccine are immunogenic generating antibody levels considered protective against smallpox, and by extrapolation, monkeypox as well. In a 2019 phase 3 efficacy trial published in the New England Journal of Medicine, 440 participants were randomly assigned to receive 2 doses of MVA (subcutaneous route) followed by one dose of the established replicating-vaccinia vaccine ACAM2000 (the MVA group) or to receive one dose of ACAM2000 (the ACAM2000-only group). MVA vaccination induced a detectable response by week 2, with neutralising antibodies peaking at week 6 (GMTs 153.5). This compares with a lower peak GMT in the ACAM2000 group at week 4 (79.3). At day 14, the GMTs induced by a single MVA vaccination (16.2) was equal to that induced by ACAM2000 (16.2), and the percentages of participants with seroconversion were similar (90.8% and 91.8%, respectively) (8).

Previous MVA vaccination has also been shown to prevent formation of a full major cutaneous reaction in the majority of participants (77.0%) after subsequent ACAM2000 vaccination, as compared with a rate of full major cutaneous reaction of 92.5% after ACAM2000 alone. The maximum lesion area of the major cutaneous reaction was significantly reduced when ACAM2000 vaccination was preceded by MVA vaccination. These results are consistent with the findings observed in persons revaccinated with traditional smallpox vaccines, who were considered to be protected against smallpox on the basis of attenuation of the major cutaneous reaction (8).

Results from a clinical study of immunocompetent individuals showed that the lower dose (0.1ml) administered intradermally was immunologically non-inferior to the standard (0.5ml) dose. 191 subjects were randomized to receive 2 intradermal doses of JYNNEOS (0.1 mL each), and 167 subjects were randomized to receive 2 subcutaneous doses of JYNNEOS (0.5 mL each), both with an interval of 4 weeks. The development of the immune response to JYNNEOS over time following subcutaneous and intradermal administration was nearly identical and the peak titres (as measured by Plaque reduction neutralisation assays (PRNT)) were non-inferior to subcutaneous administration.

There is very limited evidence on whether the vaccine can prevent or modify disease when given post-exposure. As the full course comprises 2 doses, post-exposure vaccination is unlikely to completely prevent disease, but as some immunological response to the first dose can be detected within the first 2 weeks, rapid vaccination may modify disease severity for cases with longer incubation periods (2).

Antibody persistence and boosting

There are limited data on long-term immunogenicity. At 2 years after priming vaccination with 2 doses of MVA-BN in vaccinia naïve individuals, GMT for neutralisation antibodies had fallen to 1.3 and seropositivity had declined to 5.4%. This compares with a GMT of 22 and seropositivity of 77% observed in healthy vaccinia naïve individuals after the primary course. Two small clinical studies have demonstrated that MVA-BN is able to rapidly boost pre-existing

immunological memory, induced by either licensed smallpox vaccines a long time ago or 2 years after MVA-BN. Following an MVA-BN boost 2 years after 2 doses of MVA-BN, GMT for neutralising antibodies at day 0 (pre-boost), 7 and 14 were one, 54 and 125, respectively and seropositivity was 5.4%, 92% and 99%, respectively. Two years after the booster dose, antibody levels persist for longer, with neutralising antibody GMT of 10.3 and seropositivity of 68.6% in previously vaccinated individuals (2, 6).

Following an MVA-BN boost in individuals who had received a live attenuated smallpox vaccine in the past, GMT neutralising antibodies and seropositivity were higher at baseline (day 0) at 22 and 77% and increased to 190 and 98% on day 14 (6).

Safety

Data from multiple clinical trials (9, 10, 11, 12, 13) show that MVA-BN has a favourable adverse event profile compared with first and second generation vaccines that have been studied in the pre- and post-eradication era (including the vaccines used to vaccinate groups of UK healthcare workers (HCWs) in 2003); this applies to common adverse events, such as local site reactions and influenza-like illness symptoms, as well as serious adverse events. The frequency of adverse events, particularly local site reactions, in smallpox vaccine-naïve individuals being vaccinated for the first time (with subcutaneous MVA-BN) does not appear to be significantly greater than the frequency of adverse events in revaccinees; this contrasts with the pattern observed with first and second generation vaccines (including those used in the UK). In the phase 3 clinical trial, there were fewer adverse events or adverse events of grade 3 or higher after both MVA vaccination periods in the MVA group than in the ACAM2000-only group (17 versus 64 participants with adverse events of grade 3 or higher, $P<0.001$) (8).

In a clinical study comparing intradermal (ID) and subcutaneous (SC) administration of MVA-BN, local reactions such as erythema and induration at the injection site were reported more frequently in the ID group (99.5% compared with 81.4% and 99.5% compared with 69.5% respectively). Itchiness was also more commonly reported in the ID group (89% compared with 48.5% respectively). However pain at the injection site was less commonly reported (65.4% and 91.0% respectively). Some of these local reactions persisted for longer in the ID group. For example, in the SC group erythema at the injection site was reported as resolved within 14 days following the second vaccine dose in all individuals, whereas in the ID arm 44% still had erythema at the end of this period. At Day 180, greater than a third of subjects in the ID group continued to have minimal induration or erythema present on examination. Additionally, a few patients in the ID arm developed small nodules or discoloration at the injection site. Systemic reactions were generally similar across both groups.

Use in children

Although the MVA-BN vaccine is not licensed in children, several paediatric studies of other vaccines using MVA as a vector (often at a considerably higher dose than used in Imvanex)

have been undertaken with a reassuring side effect profile. In a TB vaccine trial of approximately 1500 infants, aged approximately 5 to 6 months, MVA85A (14) at a dose of 1 x 10^8 pfu, this dose was very well tolerated. In a trial of 100 Gambian infants who received MVA85A (15) at a dose of 5 x 10^7pfu and in a further study of 100 infants who received MVA-malaria (16) at a dose of 1-2 x 10^8 pfu, there was a tolerable safety profile. The adverse event profile with MVA-BN would be expected to be identical to the profile with these TB and malaria candidate vaccines and therefore provides some reassurance of its use in children. Administration of MVA-BN in children should be through the subcutaneous or intramuscular route, as there is no evidence on the use of intradermal fractional doses in children.

Use in pregnancy

MVA-BN is not contraindicated in pregnancy. Although it has not formally been evaluated in pregnancy, animal studies (3 studies in female rats) identified no vaccine related fetal malformations. Use of MVA-BN in pregnant women is limited to fewer than 300 pregnancies without leading to any adverse events on pregnancy (6). As it is a non-replicating vaccine, there is no theoretical reason for concerns in pregnancy and the adverse events profile would be expected to be similar to that in non-pregnant vaccinees. Whilst there is not currently formal regulatory approval for use in pregnancy, any theoretical risk needs to be weighed against the maternal risks of exposure to monkeypox in late pregnancy (such as risk of more severe disease from viral infections in third trimester) and any consequent fetal risks from maternal infection in early pregnancy. Administration of MVA-BN in pregnancy can be through the subcutaneous, intramuscular or intradermal route.

Breast-feeding

MVA-BN is not contraindicated if breast-feeding. It is not known whether MVA-BN is excreted in human milk, but this is unlikely as the vaccine virus does not replicate effectively in humans. Individuals who are breast feeding and have a significant exposure to monkeypox should therefore be offered vaccination, after discussion about the risks of monkeypox to themselves and to the breast-fed child.

Individuals with underlying medical conditions (including immunosuppression and HIV)

Individuals with atopic dermatitis are known to have developed more site-associated reactions and generalised symptoms following MVA-BN vaccination. A non-placebo controlled clinical trial found that erythema (61.2% versus 49.3%) and swelling at the injection site (52.2% versus 40.8%), headache (33.1% versus 24.8%), myalgia (31.8% versus 22.3%), chills (10.7% versus 3.8%), nausea (11.9% versus 6.8%), and fatigue (21.4% versus 14.4%) were all reported at a higher frequency in participants with atopic dermatitis than in healthy participants. In vaccinated clinical trial participants with atopic dermatitis, 7% experienced exacerbation of their condition

during the course of the trials. Individuals in this group therefore need to have a risk assessment before being offered vaccination to balance the risk from exposure and the risk of side effects from vaccination (6).

The Committee for Medicinal Products for Human Use acknowledged that, compared with replication-competent smallpox vaccines, there would likely be a reduction in adverse reactions with MVA-BN, as this is largely replication-incompetent in humans. MVA-BN is therefore considered safe even in immunosuppressed individuals (17). Clinical trials on the use of MVA-BN including in immunocompromised individuals, including people with HIV, did not observe an increase in adverse events in this group (6). CDC recommends that MVA-BN can still be used in individuals who are severely immunosuppressed, for example those with recent haematopoietic stem-cell transplant (HSCT) and people with HIV who have a low CD4 count (18). However, there may be a reduced response to vaccine in people with immunosuppression and so additional precautions may be needed.

Table 1. Recommendations for pre- and post-exposure use of MVA-BN (6)

	Individuals (18 years and above) previously not vaccinated against smallpox	**Individuals (18 years and above) previously vaccinated against smallpox**	**Children under 18 years**
Immunocompetent individuals (including people with atopic dermatitis and people living with HIV with a CD4 count >200 cells/mm^3 AND virally suppressed)	0.5ml subcutaneous / intramuscular injection or 0.1ml intradermal injection (during supply constraints) + 0.5ml subcutaneous / intramuscular injection at any time from 28 days or 0.1ml intradermal injection at any time from 28 days	0.5ml subcutaneous / intramuscular injection or 0.1ml intradermal injection (during supply constraints)	0.5ml subcutaneous / intramuscular injection + 0.5ml subcutaneous / intramuscular injection at any time from 28 days
Immunosuppressed individuals (as defined in the Green Book) and those with a history of developing keloid scarring	0.5ml subcutaneous / intramuscular injection + 0.5ml subcutaneous / intramuscular injection at any time from 28 days	0.5ml subcutaneous / intramuscular injection	0.5ml subcutaneous / intramuscular injection + 0.5ml subcutaneous / intramuscular injection at any time from 28 days

Post-exposure prophylaxis for monkeypox (PEP)

The use of vaccination after an exposure to monkeypox may prevent or attenuate the infection. In the US, the Advisory Committee on Immunization Practices (ACIP) recommends that persons with an orthopoxvirus exposure should be evaluated by a health care provider and clinical management decisions, including post-exposure vaccination should be made on a case-by-case basis in consultation with public health authorities (19).

If vaccination is to be used, the CDC advises that smallpox vaccine be given within 4 days from the date of exposure to prevent onset of the disease but should be offered up to 14 days post-exposure. Administration of vaccine within 14 days of exposure, may reduce the symptoms of disease, but may not prevent disease (20). The CDC recommendations are based on their use of ACAM2000, which is a second-generation smallpox vaccine, with a different side-effect profile to MVA-BN.

Experience of use of MVA-BN vaccine in previous incidents in the UK

In 2018 and 2019, several cases of imported monkey pox were reported in the UK and MVA-BN vaccine was offered as part of the incident response, including to children. In 2018, 3 cases of monkey pox were diagnosed in the UK, and MVA-BN vaccine was offered as post-exposure vaccination to 17 community contacts (uptake of 5 out of 17; 29%). No onward transmission was identified from the first case. A total of 147 individuals at occupational risk (including healthcare workers and decontamination staff) were offered MVA-BN, (uptake of 126 out of 147; 85.8%), demonstrating high acceptability of vaccine. Following PEP, one case was identified in a healthcare worker who had received post-exposure vaccine 6 to 7 days after initial exposure. In 2019, following another imported case, 17 of 18 category 2 and 3 contacts accepted post-exposure vaccination. In these incidents, young children, including infants, have received post-exposure vaccine with no known adverse events.

Recommendations

On the basis of the current available evidence, an UKHSA (previously PHE) convened expert working group has made the following recommendations for the use of the MVA-BN vaccine during an incident.

Whilst the priority is to ensure appropriate PPE is worn, MVA-BN may be offered to provide additional protection, depending on the nature and timing of exposure risk, as described below. Details of the risk exposure classifications referred to below can be found in the Contact Management SOP in the duty doctors' pack and in the contact tracing classification and vaccination matrix for the monkeypox 2022 outbreak.

1. Pre-exposure vaccination for occupational exposure

The majority of those at risk of occupational monkeypox exposure in the UK are likely to be naïve to smallpox. In line with current policy in the 'Green Book: Immunisation against Infectious Disease' (1), naïve individuals at risk of exposure on the basis of an occupational health assessment, pre-exposure vaccination with 2 doses of MVA-BN with a minimum interval of 28 days is recommended. This would include those HCWs due to care for a patient with confirmed monkeypox, for example staff in HCID centres and those individuals undertaking environmental decontamination, even if they will be wearing full PPE.

In light of the evolving epidemic in the gay, bisexual and other men who have sex with men (GBMSM) population during the May 2022 monkeypox outbreak, UKHSA advised that pre-exposure vaccination should be extended to a wider group of staff outside of HCID units including:

- designated staff in additional hospital units being stood up to care for monkeypox patients
- staff in sexual health clinics designated to assess suspected cases

Other health care staff, including those in front line roles, should be able to avoid inadvertent exposure by ensuring that suspected monkeypox cases are triaged to be assessed by the designated staff or by wearing appropriate personal protective equipment.

Although data on use of MVA-BN in immunosuppressed patients are reassuring and the vaccine is not contraindicated in this group, individuals who are known to be severely immunosuppressed should not routinely participate in the care of a patient with a high consequence infectious disease, such as confirmed monkeypox, and therefore these groups are unlikely to require pre-exposure vaccination.

The complete vaccine course with MVA-BN in immunocompetent individuals is 2 doses given at least 28 days apart. In the event of an incident, it is highly unlikely that there will be sufficient time to offer pre-exposure vaccination with 2 doses for those at risk of occupational exposure; in this scenario a single dose of vaccine should be offered immediately. Completion of the primary course with a second dose at least 28 days later should be considered on assessment of ongoing risk of exposure and will be subject to availability of supply and prioritisation of stock during an outbreak response.

For individuals with a history of receiving a single dose of a live smallpox vaccine, a single dose of MVA-BN is recommended.

If vaccine cannot be given before commencing work with potential exposure to monkeypox, post-exposure use of vaccine is likely to be advised (see below).

Table 1 summarises MVA-BN vaccine recommendations based on prior vaccine history.

2. Post-exposure vaccination

Individuals should be risk assessed and offered post-exposure vaccination with a single dose of MVA-BN according to the Contact Management Matrix and SOP, available in the duty doctors' pack and in the contact tracing classification and vaccination matrix for the monkeypox 2022 outbreak.

Vaccination should be administered as soon as possible and within 4 days after an identified exposure to prevent or attenuate infection. Vaccination has been used up to 14 days post-exposure in earlier UK incidents, based on a theoretical possibility of attenuating disease if it occurs towards the end of the range of incubation period. However in the context of a rapidly expanding outbreak and limited supply, post-exposure vaccination should be given to all contacts ideally within 4 days. Post-exposure vaccine may be extended up to 14 days for those at high risk of ongoing exposure, for example GBMSM in the 2022 outbreak, and some HCWs where the dose will act as their first pre-exposure dose, as well as those at risk of more severe disease such as children under 5 years of age, pregnant women and immunosuppressed individuals. If exposure has been intermittent or continuous, post-exposure vaccination should ideally be given within 4 days of the last exposure.

For individuals with a history of receiving a single dose of a live smallpox vaccine, a single dose of MVA-BN is recommended.

For individuals who have received a single dose of MVA-BN previously (regardless of timing), completion of the primary course is recommended. There is no need to restart the course.

For individuals who have received a previous live smallpox vaccine and one MVA-BN vaccine, no further doses are recommended.

For individuals who have received 2 doses of MVA-BN within the last 2 years, no further doses are recommended.

For individuals who have received 2 doses of MVA-BN more than 2 years ago, a single booster dose of MVA-BN is recommended.

Table 1 summarises MVA-BN vaccine recommendations based on vaccine history.

a) Community exposure

Individuals with a community exposure should be offered post-exposure vaccination if they are in risk categories 2 and 3. Individuals with a category 1 exposure do not usually require vaccination (see the contact tracing classification and vaccination matrix for the monkeypox 2022 outbreak).

b) Occupational exposure

Individuals with an occupational exposure (for example HCWs or those undertaking environmental decontamination) should be offered post-exposure vaccination if they are in risk categories 2 and 3. Individuals with a category 1 exposure do not usually require vaccination (see the contact tracing classification and vaccination matrix for the monkeypox 2022 outbreak).

Completion of the course with a second dose at least 28 days later or any time after should be considered on assessment of a foreseeable future risk through work beyond the current episode and based on availability of stock and prioritisation of supply during an incident response.

Current or previous monkeypox infection

If an individual is acutely unwell, including those with symptoms or signs of possible monkeypox infection, immunisation should be postponed until they have fully recovered. This is to both reduce the risk of exposing others and to avoid wrongly attributing any signs of symptoms to the adverse effects of the vaccine.

3. Laboratory workers

Risk of exposure will be dependent on the nature of the setting. For example, whilst laboratory workers in containment level 3 labs (for example UKHSA Porton staff) who will handle samples from suspected cases may have already be vaccinated, those working in routine diagnostic laboratories are likely to be naïve. Workers in laboratories where pox viruses (such as monkeypox or genetically-modified vaccinia) are handled or cultured, and others who work in highly specialist laboratories undertaking procedures with a significantly higher risk of exposure, are recommended for pre-exposure vaccination. Individuals working in diagnostic laboratories, including those undertaking monkeypox PCR and/or serology, should be using standard

protective equipment and safety cabinets, and therefore the risk of exposure, even in high incidence areas, should be minimal.

Laboratory workers who experience category 2 or 3 exposures (see the contact tracing classification and vaccination matrix for the monkeypox 2022 outbreak) should be offered vaccination, following an occupational health assessment.

Completion of the course with a second dose at least 28 days later should be considered on assessment of a foreseeable risk through work and based on availability of stock and prioritisation of supply during an incident response.

4. Individuals with underlying conditions, including immunosuppression and HIV

Individuals with atopic dermatitis are known to have developed more site-associated reactions and generalized symptoms following MVA-BN vaccination. Individuals in this group therefore need to have a risk assessment before being offered vaccination to balance the risk from exposure and the risk of side effects from vaccination.

MVA-BN is a replication defective virus and should pose no risk to those who are immunosuppressed. MVA-BN vaccine has been demonstrated to be safe in people with HIV, and so they should be offered vaccine according to recommendations. However, the immune response to the vaccine could be reduced in immunosuppressed individuals. Vaccination should proceed using a 0.5ml SC/IM dose in individuals with immunosuppression (as defined in the Green Book) as they are at significant risk of the complications of monkeypox, and data on intradermal administration is absent in this population. Intradermal administration of MVA-BN can be used for individuals living with HIV with a CD4 >200 cells/mm^3 **and** who are virally suppressed.

Specialist advice on other measures may be required and additional doses should be considered for those at ongoing risk of exposure.

For individuals with a history of keloid scarring, subcutaneous or intramuscular administration of MVA-BN is recommended.

5. Prioritisation of vaccine stock during an incident

When supplies are limited, vaccine should be prioritised according to whether it is for pre- or post-exposure use, the risk and timing of exposure and the ability to benefit. In an outbreak scenario, vaccine supply should be generally prioritised for pre-exposure in the highest risk groups before post exposure use.

In June 2022, UKHSA launched its vaccine strategy for the outbreak in gay, bisexual and other men who have sex with men (GBMSM), which was endorsed by JCVI. This advised that, in the context of constrained vaccine supply, a reactive selective vaccination strategy with the aim of interrupting transmission in the subset of individuals at increased risk of exposure should be deployed. This approach was considered to be the best way to bring the current outbreak under control.

JCVI proposed that vaccination should be offered as soon as feasible to those gay, bisexual and other men who have sex with men (GBMSM) at highest risk of exposure. The initial priority is to deliver first doses to as many GBMSM in the highest risk group as possible as early as is achievable with available supply with the intention of interrupting transmission.

As most healthcare staff can be protected by adequate personal protective equipment, first dose use in staff should be restricted to those providing very close prolonged care or likely to be very frequently exposed to suspected cases during the course of an incident.

Amongst the contacts being offered post exposure vaccination, vaccination should be prioritised for groups at higher risk of severe disease including children under 5 years of age, pregnant women (especially those in the third trimester) and immunosuppressed individuals. In addition, those at high risk and therefore eligible for pre-exposure may be offered post-exposure vaccination, for example GBMSM with multiple sexual partners should be prioritised for vaccine.

Those whose last exposure is within 4 days, should be prioritised over those exposed 4 to 14 days previously. This is because post exposure vaccination is likely to be most effective when given as soon as possible.

During periods of national supply constraints, the following are recommended:

- post exposure vaccination of community contacts should be restricted to contacts in these groups (children under 5 years, immunosuppressed individuals and pregnant women) with a category 3 exposure. (See the contact tracing classification and vaccination matrix during 2022 monkeypox outbreak).

- consider intradermal administration (0.1ml) as an option, where feasible, for first and/or second doses in any adults aged 18 years and above (excluding immunosuppressed individuals – see section 4). Children under 18 years should be vaccinated either through subcutaneous or intramuscular injection. Intradermal immunisation should be administered by staff with training in the technique.

In due course, if sufficient vaccine supplies allow and subject to the evolving epidemiology, a second dose may be advised around 2 to 3 months later to provide longer lasting protection for those at ongoing risk of exposure. Vaccine will also be considered for those with a history of previous monkeypox infection and individuals eligible for a booster dose.

6. Completing the primary vaccine course

The licensed primary course of MVA-BN comprises 2 doses, given at least 28 days apart. If there is a foreseeable risk of subsequent occupational exposure to monkeypox, HCWs, laboratory workers, and individuals undertaking environmental decontamination in exposure categories 2 and 3, who have received one dose of MVA-BN either as pre- or post-exposure prophylaxis, should be offered a second dose at least 28 days after the first or any time after to complete the manufacturer-recommended schedule. This should be undertaken when supplies allow.

For those staff at occupational risk who have received a single dose of MVA-BN or a different smallpox vaccine at any time in the past, only one further dose of MVA-BN is required to complete the recommended schedule, with a minimum interval of 28 days between doses.

There is no requirement to restart the 2-dose schedule. Individuals are considered protected 7 days after completing their second dose of MVA-BN.

Individuals who received a single dose of vaccine as a result of community exposure, (regardless of exposure category), do not need to be offered a second dose as they do not have a foreseeable risk of further exposure to monkeypox and will be past the incubation period from the exposure that warranted post-exposure vaccination.

Table 2 summarises the advice for the completion of MVA-BN course and need for exclusion or isolation based on prior vaccine status (see page 13).

7. Reinforcing (booster) doses

There are limited data to determine the need and timing of a booster dose after a 2-dose primary course of MVA-BN for those at ongoing occupational risk of monkeypox. Studies have demonstrated a rapid boosting response following a single booster in individuals who have completed a primary schedule, demonstrating ongoing memory and persistence of antibodies to 24 months.

Given the evidence of immunological memory from 2 priming doses and the incubation period of monkeypox, it is likely that adequately primed individuals will make a good response to natural exposure that will protect or reduce the severity of any breakthrough infection. As the response to a booster is good and leads to better persistence, however, a single booster dose at 2 years may be considered for pre-exposure use in individuals who have received 2 doses of MVA-BN and are at ongoing high risk of occupational exposure or for post-exposure use amongst contacts who have had a significant exposure (category 2 or 3).

The data does not support giving a booster dose of MVA-BN in those who have had one dose of MVA-BN and a different smallpox live vaccine in the past. Table 2 summarises MVA-BN reinforcing dose (booster) recommendations based on prior smallpox vaccine history. Long term immunogenicity studies are in progress. If a booster dose is considered necessary, then a single dose of 0.5 ml should be administered.

Table 2. Recommendation of MVA-BN vaccination and booster doses based on vaccine history for those at occupational foreseeable risk of exposure

	Immediate advice	Exclusion or isolation advice*	Follow up from 28 days and any time after*	Follow up at 2 years
No previous vaccine	First dose	Yes	Second dose	Boost
Previous live vaccine (not MVA-BN)	First dose	No	None	None
Previous single dose of MVA-BN	Second dose	Yes	None	Boost
Previous complete course of MVA-BN less than 2 years ago	None	No	None	Boost
Previous complete course of MVA-BN 2 or more years ago	Boost	No	None	None

See section 5 on prioritisation if supplies are limited.

* See the monkeypox contact tracing classification and vaccination matrix by category exposure during the 2022 outbreak.

8. Vaccine prescribing and administration

The vaccine is licensed in Europe for use against smallpox, so, as well as having the data to support safety and efficacy in accordance with the license, the vaccine will have been manufactured to a high standard and have undergone independent batch testing before release. The vaccine has recently been authorised for protection against monkeypox in Europe; however, for the current UK stock this indication is still considered ‘off-label’. Off-label use of vaccines and other medicines can be undertaken on the basis of additional evidence or expert opinion. In this instance, there is no alternative UK licensed vaccine for the management of monkeypox and the US FDA approval of MVA-BN for the management of monkeypox indicates that there is a sufficient rationale for using the medicine for this indication.

Furthermore, animal studies have demonstrated that vaccination with MVA-BN protected non-human primates from severe disease associated with a lethal challenge of monkeypox virus. Healthcare workers can therefore be reassured that prescribing and administering MVA-BN for monkeypox in accordance with these guidelines would be in line with best practice.

Where expert guidance practice supports the use of a medicine outside the terms of its licence, it is not always necessary to draw attention to the licence when seeking consent. However, it is good practice to give as much information as patients or carers require or which they may see as relevant – a patient information leaflet is available for this purpose.

The vaccine can be given by sub-cutaneous or intramuscular injection in a dose of 0.5ml or as an intradermal injection in a dose of 0.1ml for adults aged 18 years and above.

9. Publications for the programme

Pre-vaccination checklist for healthcare professionals when assessing a person for vaccination against monkeypox using the MVA-BN (Modified Vaccinia Ankara – Bavarian Nordic) smallpox vaccine is available to download.

Consent forms as a word document or open source document and available to download and print if required.

Protecting you from monkeypox – MVA vaccination leaflet

The MVA vaccination leaflet is an essential part of the consent process and provides the patient with important information pre- and post-vaccination. It explains about the MVA vaccine and how it is being used to protect people at risk of monkeypox including a link to the product information leaflet from the manufacturer, eligibility and who the vaccination is offered to, about the vaccination, those who may not respond as well to the vaccine, information for close contacts offered the vaccination, the side effects, and how to report them to the Yellow card scheme.

Every eligible patient should be invited with a copy of the patient information leaflet. You can insert or attach the leaflet pdf or link to the HTML version of the leaflet if using texts or emails to invite patients.

It is important to give patients the information in an accessible format and we offer the leaflet in the translations listed below and in Braille and large print are now available to order as paper copies. The British Sign Language (BSL) video is available to signpost to or to download.
You can now place orders for translated versions of the monkeypox leaflet in Albanian, Arabic, Bengali, Estonian, French, German, Hindi, Latvian, Lithuanian, Panjabi, Polish, Portuguese, Romanian, Russian, Spanish, Swahili, Tigrinya, Ukrainian, Urdu, Xhosa and Yoruba.

Monkeypox MVA vaccination record card – pack of 25 cards

Every patient vaccinated should also be given a Monkeypox MVA vaccination record card with their name and the batch number of the vaccine that they are given. Monkeypox MVA vaccination record card – packs of 25 cards are available to order using product code 2022MPX6.

'Why do I have to wait for my Monkeypox vaccine?' leaflet

It is helpful for all sexual health services and occupational settings who are either offering the vaccine or unable to offer the vaccine and are signposting to other services to have a stock of the why do I have to wait for my vaccine leaflet. This leaflet is for eligible patients who have to wait for the second dose, for patients and healthcare workers who are not currently eligible.

Paper copies of this leaflet are available free to order using product code: 2022MPX3

An HTML version and PDF are available if you want to link to it in an invitation or text.

Intradermal monkeypox vaccination – what you need to know

Paper copies of this leaflet are available free to order using product code: MPXIDEN

Intradermal monkeypox vaccination – guide for eligible patients leaflet

If you are offering the MVA vaccination intradermally, each patient should be given a copy of this leaflet as it explains the technique and the fractional dose to the patient, invites them to be part of the post-vaccination survey and gives them the information they need to consent to the intradermal vaccination.

Copies can be ordered using product code MPXIDEN and you can download the pdf or HTML.

10. How to order stocks of the leaflets and record cards

All the vaccination programme publications are available to order from the Health publications website. Once you have registered as a clinic or NHS provider you can place orders for 500 to 1,000 copies of any publications. You can also place orders by calling 0300 123 1002 (9am to 5pm Monday to Friday). This is a free service with free delivery. In stock items take 3 to 5 working days to arrive. All sites delivering the vaccinations and sites unable to deliver the vaccines can order stocks of the vaccination resources. There are also human papillomavirus (HPV) vaccination publications and other programme resources which may be helpful for specialist sexual health providers and trusts.

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About the UK Health Security Agency

UKHSA is responsible for protecting every member of every community from the impact of infectious diseases, chemical, biological, radiological and nuclear incidents and other health threats. We provide intellectual, scientific and operational leadership at national and local level, as well as on the global stage, to make the nation health secure.

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