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Smallpox and monkeypox

NOTIFIABLE

The disease

Smallpox

Smallpox is a highly transmissible disease which was one of the most severe infectious diseases affecting humans. Smallpox (variola) virus is a DNA virus, and a member of the genus *orthopoxvirus* of the Poxviridae family, which also includes vaccinia and monkeypox. In December 1979, the Global Commission for the Certification of Smallpox Eradication declared the world free of smallpox and this declaration was ratified by the World Health Assembly in May 1980.

Monkeypox

Monkeypox is a rare disease that is caused by infection with the monkeypox virus. Monkeypox virus is related to but distinct from the viruses that cause smallpox (variola virus) and cowpox. The name monkeypox originates from the initial discovery of the virus in monkeys in a Danish laboratory in 1958.

Human monkeypox was first described in 1970 when regional elimination of smallpox revealed sporadic cases of a disease with similar presentation in rural areas of Democratic Republic of Congo. Outbreaks have since occurred in Nigeria, Republic of Congo, Sierra Leone, Liberia, Cameroon and the Central African Republic. Monkeypox is a zoonosis - an organism transmitted to humans from animals. The animal host is most likely a rodent, although the definitive reservoir has not been identified. Following the global eradication of smallpox in 1977, monkeypox has become the dominant cause of orthopox outbreaks in humans, possibly associated with waning orthopox immunity following cessation of smallpox vaccination (Rimoin *et al.* 2010).

Spread of monkey pox may occur when a person comes into close contact with lesions, body fluids, respiratory droplets from an animal or human with the infection; or contact with material contaminated with the virus e.g. bedding. The virus enters the body through broken skin, the respiratory tract or the mucous membranes.

The incubation period is 5 to 21 days, but typically 6 to 13 days following exposure. Most patients experience a mild, self-limiting illness, with spontaneous and complete recovery seen within 3 weeks of onset. However, severe illness can occur and sometimes results in death. The risk of severe disease is higher in children, pregnant women and immunosuppressed individuals.

There are two genetic clades of monkeypox virus: Central African and West African. The Central African clade is associated with more severe disease in humans and a reported case fatality rate of up to 10%. By contrast, the West African clade is associated with milder disease, with a case fatality rate of 3-4%. Monkeypox is included in the national list of High Consequence Infectious Diseases (HCID) in England.

History and epidemiology of the disease

Smallpox

Compulsory childhood smallpox vaccination of the UK population commenced in 1853. Smallpox ceased to be endemic in the UK by the 1930s, although importations continued to occur, with outbreaks in England in 1949 and Scotland in 1950. Smallpox vaccination remained routine in infants until 1962, although coverage of vaccination had declined to low levels in many areas. Vaccination as part of outbreak control was better accepted and vaccination of older schoolchildren and adults remained until 1971, when it was replaced with a selective risk group policy (Milward G, 2019).

In response to the threat of a bioterrorist release of smallpox, in 2003 the Department of Health published *Guidelines for smallpox response and management in the post-eradication era (smallpox plan)*.¹ This outlined the role of vaccination of response teams who would safely manage and diagnose suspected cases of smallpox. In 2003–04 more than 300 healthcare and ambulance workers were vaccinated, along with a small number of staff in laboratories designated to receive specimens from suspected cases.

Monkeypox

Between 2018 and 2022 the UK experienced a small number of imported cases, all from west Africa and with the west African clade. Spread was limited by rapid diagnosis, isolation and care of the cases in HCID centres and the quarantine and surveillance of close contacts. Post exposure vaccination was also advised, and no serious consequences of disease occurred.

In April/May 2022, three separate incidents of monkeypox were recognized. The first was a recognized importation from Nigeria with no secondary spread. The second incident appeared to arise from indigenous transmission. One index case with no travel history infected two other members of the household. The third incident is still under investigation but appears to indicate transmission largely in gay, bisexual and other men who have sex with men (GBMSM). At the time of writing more than 700 cases have been confirmed, mainly in London, and the vast majority in males. The outbreak appears to be associated with cases in similar populations worldwide including Canada, Portugal, Belgium and Germany.

The smallpox vaccination

First and second generation smallpox vaccines

Historically, first and second-generation smallpox vaccines were used for population-level and targeted occupational health-related immunisation programmes in the UK. These vaccines are no longer available in the UK.

First generation smallpox vaccines used during eradication were propagated in calf skin and purified from calf lymph. A successful vaccination produced a lesion at the site of administration. Second generation vaccines were propagated in tissue cell culture and produced using modern good manufacturing practices, thus having a lower risk of contamination with adventitious agents (Petersen *et al.* 2019).

First and second generation vaccines contain a live (replicating) vaccinia virus, mostly based on either the Lister or the New York City Board of Health (e.g. ACAM2000) strains.

1 <https://webarchive.nationalarchives.gov.uk/ukgwa/20130107105354/http://www.dh.gov.uk/assetRoot/04/07/08/32/04070832.pdf>

Although these live vaccines were highly effective, they were also associated with risks of other serious adverse events (Auckland C *et al*, 2005, Gallagher and Lipsitch 2019, Lane *et al*, 1968, Mora *et al*, 2009, Morgan *et al*, 2008). Previous data from Africa suggests that the live vaccines against smallpox may also be up to 85% effective in preventing monkeypox infection.

Third generation smallpox vaccines

Newer third generation smallpox vaccines are now available which have a much-improved side effect profile compared with first and second generation smallpox vaccines. The modified vaccinia Ankara (MVA-BN) (Imvanex®) vaccine, a third generation smallpox vaccine contains a replication defective virus. The virus used in the vaccine is attenuated through multiple passages in chicken embryo fibroblast cells, leading to a substantial loss of its genome including immune evasion and virulence factors. 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 (Verheest C *et al*, 2002). As MVA-BN cannot replicate in mammalian cells it does not produce a lesion at the site of vaccination.

MVA-BN (Imvanex®) was licensed by European Medicines Agency in 2013 for the prevention of smallpox. Data used for licensing was limited due to the eradication of smallpox in 1979 followed by the requirement for containment of the virus. Preclinical studies of MVA-BN have suggested that 2 doses of vaccine are immunogenic, generating antibody levels considered protective against smallpox, and by extrapolation, against monkeypox. In addition, studies have shown that MVA-BN prevented lethal monkeypox in primate challenge models with protection occurring 6 or more days after a single vaccination (Earl *et al*, (2008). Although the vaccine contains a live virus, this virus has been modified so that it does not replicate in humans, and can only replicate in certain cell lines used for manufacture. Therefore, like vaccines that contain non-replicating vectors (such as the AstraZeneca COVID-19 vaccine), it should be considered as an inactivated vaccine (see chapter 1).

Smallpox MVA-BN vaccine has been recommended by UKHSA for off-license pre-exposure vaccination of a small number of laboratory staff and hospital health care workers at high risk for post exposure vaccination against monkeypox.

There is currently no vaccine licensed in the UK or Europe for immunisation against monkeypox. In September 2019, the Food and Drug Administration (FDA) in the US approved MVA-BN (Jynneos®) (the US labelled equivalent of Imvanex®) for the prevention of monkeypox as well as smallpox (FDA, 2019). Although not specifically licensed for the prevention of monkeypox in Europe, MVA-BN vaccine has been used in the UK in response to the current and previous incidents.

Unlike the live smallpox vaccine, there is very limited evidence on whether MVA-BN can prevent or modify disease when given post-exposure. At day 14, the GMTs induced by a single MVA vaccination was equal to that induced by a live smallpox vaccine (ACAM2000), and the percentages of participants with seroconversion were similar (90.8% and 91.8%, respectively) (Pittman *et al*, 2019). Based on this immunological response, rapid vaccination is offered because of the potential to prevent infection and/or to modify disease severity for cases with longer incubation periods.

Presentation

The vaccine comes in packs of 20 single dose vials. The vaccine's normal appearance is a light yellow to pale white milky suspension.

Storage

MVA-BN is supplied frozen in packs of 20 vials. The remaining shelf life at clinic level will depend on previous storage temperature, please refer to documentation on the product.

Frozen vials should be transferred to 2°C to 8°C to thaw or may be thawed for 15 minutes at room temperatures for immediate use. After thawing, vaccine can be stored for up to 8 weeks at 2°C to 8°C. Store in the original package in order to protect from light.

Administration

The vaccine should be allowed to reach room temperature before use. Swirl the vial gently before use for at least 30 seconds. The vaccine should be visually inspected for particulate matter and discoloration prior to administration. In the event of any foreign particulate matter and/or variation of physical aspect being observed, do not administer the vaccine.

Most vaccines should be given by intramuscular (IM) injection (see chapter 4), but the MVA-BN Summary of Product Characteristics (SmPC) advises that the vaccine should be administered by the deep sub-cutaneous (SC) route. As there is published evidence suggesting an adequate immunological response (Vollmar et al, 2006) and extensive experience of using MVA containing vaccines given by the IM route, UKHSA has advised that intra-muscular administration is an acceptable alternative. For adults, the preferred sites for both IM and SC immunisation is the deltoid area of the upper arm; for small children the anterolateral aspect of the thigh is preferred (see chapter 4).

Dosage and schedule

Pre-exposure vaccination of individuals previously not vaccinated against smallpox

Administer a course of two doses with at least a 28-day interval between doses, for instance:

- first dose of MVA-BN 0.5ml, then
- second dose of MVA-BN 0.5ml at least 28 days after the first dose

Individuals who have previously been vaccinated against smallpox with a live smallpox vaccination should receive a single dose of 0.5 ml. Live vaccine was only used up to the 1970s, so apart from the healthcare workers vaccinated in 2003/4, vaccinated individuals will be older, and should have a distinctive scar (which normally looks like a circular 5p size dent in the left upper arm).

In the event of an incident, it is highly unlikely that there will be sufficient time to offer pre-exposure vaccination with two 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. Where the second dose of MVA-BN is given after 28 days, the first dose should not be repeated.

Post-exposure of individuals of any age

Administer a single 0.5ml dose of MVA-BN.

To maximise the chance of preventing infection, MVA-BN should preferably be administered within 4 days from the date of exposure to monkeypox.

Vaccination may still be offered up to 14 days after exposure, with the aim of reducing the symptoms of disease, for those who are not already displaying symptoms. This may be considered in those at higher risk of serious monkeypox infection (children under five years of age, the immunosuppressed and pregnant women). Vaccination up to 14 days after exposure may also be offered to those at on-going risk to commence a pre-exposure course.

Individuals who have previously received a two dose course of MVA-BN, with the second dose given in the past two years, do not need a further dose of vaccine after exposure. The exception is those who are immunosuppressed, who may have made a lower or less durable immune response, when an additional dose can be considered.

Booster vaccination

Immunocompetent individuals who have previously been vaccinated against smallpox should receive a single 0.5ml dose of MVA-BN, no less than two years after the primary course if they are considered to be at on-going risk or in the event of an exposure incident.

Disposal

Equipment used for vaccination, including used vials, ampoules or syringes, should be disposed of by placing them in a proper, puncture-resistant 'sharps box' according to local authority regulations and guidance in Health Technical Memorandum 07-01: Safe management of healthcare waste (Department of Health, 2013).

MVA-BN (Imvanex®/Jynneos®/Imvamune®) contains an attenuated organism. Sharps waste and empty vials should be placed into yellow lidded waste bins and sent for incineration; there is no designation as GMO waste.

Recommendations for the use of MVA-BN smallpox vaccine**Pre-exposure immunisation**

The objectives of immunisation are to provide protection in adults at high risk of exposure to monkeypox or other orthopox viruses.

Given the low incidence of infection in the UK, most workers are at very low risk of exposure to monkeypox, so do not require routine pre-exposure vaccination. Unvaccinated staff who are required to see suspected cases should wear full personal protective equipment and avoid direct and close contact.

Staff who work in specialist roles where exposure to orthopox is likely to be more common, should be advised of the possible risk and offered vaccination on the basis of an occupational health risk assessment. This would include:

- workers in laboratories where pox viruses (such as monkeypox or genetically modified vaccinia) are handled, and others whose work in specialist and reference laboratories with an identifiable risk of exposure (Advisory Committee on Dangerous Pathogens and the Advisory Committee on Genetic Modification, 1990). Individuals working in diagnostic laboratories should be using standard protective equipment and safety cabinets and therefore the risk of exposure, even in high incidence areas, should be minimal.

- staff working in High Consequence Infectious Disease (HCID) units
- staff regularly undertaking environmental decontamination around cases of monkey pox

Pre-exposure vaccination may also be considered for those about to start to provide prolonged or close care for a patient with confirmed monkeypox.

Pre-exposure use in outbreaks and incidents

In situations of on-going community transmission in the UK, MVA-BN may be considered for use in a wider population at potential risk. This includes extension of pre-exposure vaccination recommendations to protect additional health care staff outside of HCID settings who are more likely to see cases in settings or populations where the outbreak is happening. It may also include any population in which community transmission has been detected, and where standard infection control and follow up is challenging and likely to be ineffective. This would include, for example, a population with a large number of unidentified or anonymous contacts, residential settings where isolation was challenging, such as prisons and care homes, or excluded populations who may not be able to access care (such as homeless populations).

In the May 2022 monkeypox outbreak, UKHSA has therefore 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 avoid exposure by ensuring that suspected monkeypox cases are triaged to be assessed by the designated staff or by wearing appropriate personal protective equipment.

In June 2022, JCVI advised that a reactive selective vaccination strategy with the aim of interrupting transmission in the subset of individuals at increased risk of exposure should be deployed. They concluded that this would be 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. Subject to the evolving epidemiology, a second dose may be advised around 2-3 months later to provide longer lasting protection.

The committee agreed that GBMSM at highest risk could be identified amongst those who attend sexual health services, using markers of risk similar to those used to assess eligibility for HIV pre-exposure prophylaxis (PrEP), but applied regardless of HIV status. These risk criteria would include a recent history of multiple partners, participating in group sex, attending sex on premises venues or a proxy marker such as recent bacterial sexually transmitted infection (in the past year).

UKHSA have also advised that vaccination may also be offered to staff members who work in sex on premises venues, such as saunas, if they are regularly exposed to items (e.g. linens) or surfaces likely to be contaminated with body fluids or skin cells. This offer could be combined with supplementary approaches to provide outreach vaccination to high risk

GBMSM who may not be in contact with sexual health services. Data from the Reducing Inequalities in Sexual Health during the COVID-19 pandemic (RiSH-COVID; unpublished) suggests that this accounts for around 10% of GBMSM.

Post exposure vaccination

The objectives of immunisation are to provide protection against infection and to modify disease severity in individuals of any age with recent exposure to monkeypox. Post-exposure vaccination of high risk community or occupational contacts is offered, ideally within 4 days of exposure, although may be offered up to 14 days in those at on-going risk (for example during an outbreak) or those who are at higher risk of the complications of monkeypox – this includes children below the age of five years, pregnant women and individuals with immunosuppression.

Previous incomplete vaccination

If the MVA-BN course is interrupted or delayed, it should be resumed using the same vaccine but the first dose does not need to be repeated.

Evidence suggests that those who have previously received a live smallpox vaccine make an antibody response to their first dose of MVA-BN as good or better than after a second dose of MVA-BN in naïve individuals. Anecdotal reports during management of the early imported cases reported in the UK suggests that healthcare workers vaccinated with the Lister/Elstree vaccine in 2003/4 experienced a higher rate of the common side effects, particularly local reactions, after their first dose of MVA-BN. This suggests that live vaccines prime very effectively for immunity and that a single dose of MVA-BN is sufficient to complete a primary course, regardless of interval since receipt of the live vaccine.

Reinforcing vaccination

There are limited data to determine the appropriate timing of booster doses. Studies two years after the second primary dose showed a decline in antibody levels and a fall in the proportion of people with neutralizing antibody. A booster dose given two years after the primary course increases the proportion of recipients with measurable antibody and this appears to be sustained at higher levels two years later.

Where boosting is considered necessary for those at on-going risk of exposure, a single dose of 0.5 ml should be administered, at least two years after the primary course. If a documented exposure occurs more than two years after the primary course, a single dose of 0.5 ml should be administered within 4 days.

In individuals who have received a dose of live vaccine followed by a single dose of MVA-BN, the need for further boosting is unclear. For those at on-going risk of exposure, a booster of MVA-BN may be considered two years after the previous dose of MVA-BN, or, after that, at the time of an additional exposure.

Co-administration with other vaccines and prophylaxis

Although no data for co-administration of MVA-BN vaccine with other vaccines exists, in the absence of such data first principles would suggest that interference between inactivated (non-replicating) vaccines with different antigenic content is likely to be limited (see Chapter 11). Based on experience with other vaccines, any potential interference is most likely to result in a slightly attenuated immune response to one of the vaccines. There is no evidence of any safety concerns, although it may make the attribution of any adverse events more difficult.

Inactivated (or non-replicating) vaccines such as MVA-BN can also be co-administered with live vaccines and in those on HIV PrEP.

As the non-replicating MVA-BN is considered inactivated, where individuals in an eligible cohort present having recently received one or more inactivated or another live vaccine, MVA-BN vaccination should still be given. The same applies for most other live and inactivated vaccines where MVA-BN vaccination has been received first or where a patient presents requiring two or more vaccines. It is generally better for vaccination with any required vaccines (including MVA-BN, hepatitis A, hepatitis B and HPV) to proceed to avoid any further delay in protection and to reduce the risk of the patient not returning for a later appointment.

Contraindications

The vaccine should not be routinely given to individuals who have had a previously had a sudden life-threatening allergic reaction to a previous dose of MVA-BN or to any ingredient of MVA-BN. MVA-BN includes trace residues of chicken protein, benzonase, gentamicin and ciprofloxacin from the manufacturing process.

Precautions

Minor illnesses without fever or systemic upset are not valid reasons to postpone immunisation. If an individual is acutely unwell, immunisation may be postponed until they have fully recovered. This is to avoid confusing the differential diagnosis of any acute illness by wrongly attributing any signs or symptoms to the adverse effects of the vaccine.

Pregnancy

Although MVA-BN has not formally been evaluated in pregnancy, animal studies (three studies in female rats) identified no vaccine related fetal malformations. Use of MVA-BN in pregnant women is limited to less than 300 pregnancies without leading to any adverse events on pregnancy. 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 it is not routinely recommended for use in pregnancy, any theoretical concern needs to be weighed against the maternal risks from monkeypox in pregnancy (such as a risk of more severe disease from viral infections in the third trimester) and any consequent fetal risks from maternal infection in early pregnancy.

Breastfeeding

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

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. The assessment should consider the risk of exposure, the risk of side effects from vaccination and the potential use of alternative preventive interventions.

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 risks of exposing others and to avoid wrongly attributing any signs or symptoms to the adverse effects of the vaccine.

Whether prior monkeypox infection protects against future infection is currently unknown, but based on analogy from smallpox infection and from live smallpox vaccine, it seems likely that re-infection will be unusual, particularly in the short term. Although previous monkeypox infection is not a contra-indication to vaccination, in a situation of constrained vaccine supply, it is therefore recommended that vaccination of confirmed cases is deferred. If supply allows, vaccination may be considered those at on-going risk once fully recovered.

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 MVA-BN) have been undertaken with a reassuring side effect profile. This includes a TB vaccine trial of approximately 1500 infants, aged approximately 5 to 6 months, and a trial of 200 Gambian infants who received an MVA malaria vaccine with an acceptable safety profile (Tameris *et al*, 2013, Oto *et al*, 2011, Afolabi *et al*, 2016). 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, including infants. The vaccine should therefore be offered to children considered to be at risk, as children seem to have a more severe presentation of monkeypox.

Immunosuppression including HIV infection

MVA-BN is a replication defective virus and should pose no risk to those who are immunosuppressed. The safety and immunogenicity of MVA-BN in persons living with HIV infection (with CD4 cell counts above 100 cells/mm³) has been demonstrated (Greenberg *et al*, 2013). However, the immune response to the vaccine could be reduced in severely immunosuppressed individuals. Vaccination should generally proceed in accordance with recommendations, as individuals with immunosuppression are also at significant risk of the complications of monkeypox. Specialist medical advice on other measures may be required and additional doses should be considered for those at ongoing-risk of exposure.

Adverse Reactions

Data from multiple clinical trials shows that MVA-BN has a favourable adverse event profile compared with first and second generation smallpox vaccines (WHO 2013, Frey *et al*, 2007, Vollmar *et al*, 2006, von Krempelhuber *et al*, 2010, Greenberg *et al*, 2013). Common adverse events include local site reactions and influenza-like symptoms. These events were mainly mild to moderate in intensity and resolved without intervention within seven days following vaccination. Adverse event rates reported after either vaccination dose (1st, 2nd or booster) were similar, but anecdotally the frequency of adverse events, particularly local site reactions, appears to be higher in those who had receive previous live smallpox vaccine.

Unlike the live vaccine, there have been no reports to date of myocarditis/pericarditis or encephalitis after these vaccines.

Live smallpox vaccine

No live smallpox vaccine is licensed for use in the UK, and there is no current indication for live smallpox vaccination for any individual. In response to the threat of a bioterrorist release of smallpox, in 2003 the Department of Health published guidelines for smallpox response and an information pack for non-emergency vaccination of first responders. The pack includes information on administration and types of vaccine. It also has guidance on pre-vaccination screening and exclusion criteria and on work restrictions following vaccination.²

Vaccination with live vaccination is no longer recommended for people exhuming bodies in crypts, since the theoretical risk involved poses less risk than the live vaccine.

Reporting anaphylaxis and other allergic reactions

Anaphylaxis is a very rare, recognised side effect of most vaccines and suspected cases should be reported via the Yellow Card Scheme (www.yellowcard.mhra.gov.uk). Chapter 8 of the Green Book gives detailed guidance on distinguishing between faints, panic attacks and the signs and symptoms of anaphylaxis. If a case of suspected anaphylaxis meets the clinical features described in Chapter 8, this should be reported via the Yellow Card Scheme as a case of 'anaphylaxis'. Cases of less severe allergic reactions (i.e. not including the clinical features of anaphylaxis) should not be reported as anaphylaxis but as 'allergic reaction'.

As this vaccine is labelled with a black triangle, all adverse reactions occurring in individuals of any age after vaccination should be reported to the MHRA using the Yellow Card Scheme. Anyone can report a suspected adverse reaction to the Medical and Healthcare products Regulatory Agency (MHRA) using the Yellow Card reporting scheme (www.yellowcard.mhra.gov.uk). Any adverse reaction should also be documented in accordance with local procedures.

Management of suspected cases and contacts

Further guidance on the management of contacts and cases of monkeypox can be found at:

<https://www.gov.uk/government/collections/monkeypox-guidance>

The use of smallpox vaccine during a monkeypox incident can be found in this document published by UKHSA: *Recommendations for the use of pre and post exposure vaccination during a monkeypox incident*. It is available at

<https://www.gov.uk/government/publications/monkeypox-vaccination>.

Supplies

Imvanex® in Europe, Jynneos® in the USA and Imvamune® in Canada is manufactured by Bavarian Nordic. Vaccine is available from UKHSA. Contact UKHSA vaccine supply team.

2 <https://webarchive.nationalarchives.gov.uk/ukgwa/20130107105354/http://www.dh.gov.uk/assetRoot/04/07/08/32/04070832.pdf>
<https://webarchive.nationalarchives.gov.uk/ukgwa/20031117030644/http://www.doh.gov.uk:80/smallpox/vaccination/index.htm>

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