

Candidate Vaccines and Therapeutics against Monkeypox Infection

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Abstract

While human beings are still facing the challenges of the pandemic coronavirus disease (Covid-19), a new viral disease, monkeypox raises concerns among healthcare authorities about this new threat. Since May 2022, thousands of people have been affected by a continuous monkeypox outbreak linked to close contact transmission in numbers of nonendemic nations. The Food and Drug Administration (FDA) has not yet approved any medications to treat monkeypox in humans. However, medications created for smallpox patients, such as antivirals and other medical countermeasures, might also be effective against monkeypox. Tecovirimat (TPOXX), brincidofovir, cidofovir antivirals and Vaccinia Immune Globulin Intravenous (VIGIV) are the medical countermeasures for the treatment of monkeypox. The second and third generations of smallpox vaccinations have been developed after many years of research. Some of these vaccines may also be beneficial for monkeypox. Three vaccinations, MVA-BN, LC16, or ACAM2000 can be used for monkeypox. Two of these (MVA-BN and LC16) have received approval for the purpose of preventing monkeypox. Considering the current vaccine shortage, widespread immunisation is not advised. Therefore, prevention is the best policy to keep everyone safe. The current review highlights the treatment available for the management of monkeypox. It also reviewed the preventive measures that human beings should take to protect themselves from monkeypox infection.

Keywords: Monkeypox, Treatment, Antivirals, Vaccines, Prevention

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Citation: Nainwal N, Jakhmola V. Candidate Vaccines and Therapeutics against Monkeypox Infection. *J Pure Appl Microbiol.* 2022;16(suppl 1):3096-3105. doi: 10.22207/JPAM.16.SPL1.22

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INTRODUCTION

Monkeypox (MPOX) is a viral zoonotic illness, but human cases have been documented since 1970 and have become more common recently.¹ Monkeypox virus (MPXV) is the double-stranded DNA virus of the Orthopox genus in the Poxviridae family. Orthopox virus is of the same genus as variola that is responsible for smallpox and vaccinia viruses that is used in the smallpox vaccine.² The 200–500 nm-sized double-strand DNA monkeypox virus is encased in a lipoprotein envelope. There are 190 open reading frames in the 197 kb monkeypox genome (ORFs). Additionally, it has been suggested that the immunomodulation process may be controlled by the monkeypox genome.³ Monkeypox got its name when it was first found in 1958 in colonies of monkeys kept for research. The decision to rename the illness is still being discussed with experts. Monkeypox is not as severe clinically as smallpox. According to a report by the WHO, 3-6% of cases of monkeypox result in death. Due to its potential to spread throughout the entire world, like the coronavirus, this illness is crucial to global public health. Dr Tedros Adhanom Ghebreyesus (WHO Director-General) declared monkeypox to be a public health emergency of international concern (PHEIC) on July 23, 2022. According to the International Health Regulations, declaring a PHEIC is the highest global public health alert level and can improve coordination, cooperation, and international solidarity.⁴

Prior to 2022, Central and West Africa saw the most instances of monkeypox. However, a persistent outbreak linked to person-to-person transmission, first identified in May 2022, has affected thousands of people in several nonendemic nations. Monkeypox is currently spreading in various parts of the world where the virus has not previously been detected, including Europe, America, Africa, the Western Pacific, Eastern Mediterranean countries, and South East Asia.⁵⁻⁹ The virus of monkeypox can spread through aerosols. Monkeypox is less contagious than certain other infections as it can be transmitted only through close contact, including touching, kissing, and sex through any kind with an infected person. Children may get infected with monkeypox if they come into close touch with a person who is

exhibiting symptoms. Monkeypox patients often develop a rash that is different, but it can also resemble that of several other viral illnesses like herpes simplex infection, varicella-zoster virus infection, secondary syphilis etc.^{1,10,11}

The WHO states that the smallpox vaccine might be used to prevent and treat monkeypox. However, research towards a particular monkeypox vaccination is ongoing. WHO is working with all the countries affected to enhance surveillance, provide guidance on how to prevent the spread, as well as provide medical care.⁴

Treatment available for monkeypox

Many monkeypox patients have mild conditions and will recover on their own. However, some individuals might need to take painkillers for pain related to proctitis or tonsillitis. Stool softeners, topical lidocaine, and/or sitz baths must also be utilised for disorders like proctitis. For those who have or are at risk for dehydration (such as those with nausea, vomiting, dysphagia, or severe tonsillitis), those who need more intensive pain management, and those who are dealing with severe illness or consequences, supportive care requiring hospitalisation may be necessary. Treatment may still be beneficial for those who are immunocompromised and living with HIV. Tecovirimat, VIGIV, and brincidofovir, are currently available medical option from the Strategic National Stockpile (SNS) for monkeypox treatment.^{12,13} Cidofovir is available commercially for the treatment option.^{4,13} The management therapies for monkeypox are given in Table 1.

Antiviral therapy

There is currently no medication authorised, especially for the infection caused by the monkeypox virus. The antivirals used for smallpox patients may be helpful in treating monkeypox. Based on dose and safety studies in healthy individuals and animal models, antiviral medications were licenced for the treatment of smallpox, but it is predicted that they will work similarly against monkeypox. The preferred treatment now is tecovirimat.¹⁰

Tecovirimat (TPOXX, ST-246)

The antiviral drug Tecovirimat has been approved by the United States Food and Drug

Table 1. The management therapies for monkeypox

Therapeutic agents	Mechanism of action	Recommended dose	Route of administration
Tecovirimat (TPOXX, ST-246)	Orthopoxvirus protein inhibitor	Based on the body weight. For person weighed >40kg to <120kg 600 mg in 3 capsules in every 12 hours.	Oral, and intravenous (IV)
Brincidofovir (CMX001 or Tembexa)	Phosphorylated conversion to cidofovir that prevents viral DNA synthesis by inhibiting orthopoxvirus DNA polymerase, preferentially.	Adults > 48 kg, 200 mg twice each week; Adults and paediatric between 10 kg to 48 kg weight should take 200 mg for 2 doses one a week, while paediatric patients < 10 kg should take oral suspension at 6 mg/kg for 2 doses once in a week.	Peroral (PO) tablets, oral suspension
Cidofovir (Vistide)	Prevents viral DNA synthesis by inhibiting orthopoxvirus DNA polymerase, after undergoing cellular phosphorylation	One weekly dose of 5mg/kg for 2 weeks, followed by 5mg/kg once in every next week	Intravenous
Vaccinia Immune Globulin Intravenous (VIGIV)	Immunoglobulin derived from combined human plasma of smallpox vaccine recipients provide passive protection against infection.	Single dose vial of 20 mL containing ≥50,000 Units (U) in each vial of neutralizing vaccinia immune globulin antibodies.	Intravenous

Administration (FDA) against smallpox infection in both adults and children.¹⁴ For those with severe illness or those at risk of developing it, as well as those who have lesions in their eyes, mouth, or anogenital region, antiviral medication is advised. Despite the lack of clinical data, tecovirimat seems to be well tolerated and has the potential to decrease the length of infection and viral shedding. A clinical trial (STOMP) is currently being conducted to determine how well tecovirimat treats monkeypox.¹⁵ For pregnant and nursing women who are infected with monkeypox virus, the Centers for Disease Control and Prevention (CDC) advises antiviral treatment with tecovirimat. However, animal studies are the only source of information on the risks of tecovirimat to the foetus. In those experiments, tecovirimat was given orally to animals at doses that were roughly 23 times higher than those that are advised for humans. However, no specific foetal adverse effects were noticed.¹⁶

In children with monkeypox, tecovirimat treatment is necessary for those who have severe disease (airway obstruction, confluent lesions, encephalitis), consequences (cellulitis/abscess, ocular lesions, pneumonia, or sepsis), and lesions involving anatomic sites that could cause the major outcome, such as scarring or strictures (e.g., infections involving the eyes, face, or genitals). Children under the age of 8, children suffering eczema and other skin diseases, and immunocompromised children should all be given the option of receiving antiviral medication.¹⁰ Alternative medications, such as cidofovir or vaccinia immune globulin, must be chosen on case basis. If tecovirimat is unavailable, a person must decide whether to treat with an alternate drug such as cidofovir (or brincidofovir, if available), because these drugs carry a higher risk of side effects (eg, renal failure, electrolyte abnormalities) ¹⁰. There is limited information about tecovirimat use in humans.^{12,15,17-22}

In addition to tecovirimat, eye drops or ointments containing trifluridine (or vidarabine) can be used to treat monkeypox lesions that affect the eye or lids.²³ Tecovirimat has generally been well tolerated in people with monkeypox.²⁴ In an expanded safety experiment that was conducted on about 360 human volunteers as part of the approval procedure, tecovirimat was given, and

the results showed that the adverse effect profile was comparable to that of a placebo.²⁵ Headache, nausea, and abdominal pain are the side symptoms that are most frequently mentioned. In a study on 255 patients who got tecovirimat, the median time to subjective benefit after beginning medication was three days.²⁴ In a different group of seven monkeypox patients, the one who had tecovirimat treatment had a shorter duration of disease and virus shedding than the others, including several who received brincidofovir.¹ Its efficacy during the ongoing monkeypox outbreak is being investigated in a randomised experiment.²⁶ The majority of tecovirimat evaluation studies conducted before the 2022 monkeypox outbreak were conducted on animal models, and tecovirimat protected nonhuman primates from lethal monkeypox virus infections.¹⁶

Cidofovir

Cidofovir (Vistide), is an injection-based antiviral drug that has been given FDA approval for treating cytomegalovirus (CMV) retinitis in AIDS patients.¹⁶ The effectiveness of cidofovir against monkeypox infection in humans is not known. However, some in vitro and animal studies have shown its efficacy against orthopoxviruses.²⁷⁻²⁹ Cidofovir treatment may be considered in cases where a patient has a severe monkeypox infection, although the treatment benefits are not known. Its use can cause significant negative effects, such as nephrotoxicity.¹⁶

Brincidofovir (CMX001 or Tembexa)

Brincidofovir is an oral prodrug of cidofovir. The safety profile of brincidofovir may be better than that of cidofovir. In contrast to cidofovir treatment, serious renal damage or other side effects have not been reported when treating cytomegalovirus infections with brincidofovir. It is not advisable to use brincidofovir and cidofovir together.¹⁶ Brincidofovir was authorised for use in the United States in June 2021 to treat smallpox.³⁰ It is accessible via the FDA's emergency investigational drug (EIND) programme. There are few documented studies on the effectiveness of this antiviral drug against monkeypox virus. It is probably a successful treatment for orthopoxvirus infections, according to animal studies.³¹⁻³³ However, three monkeypox patients were given

brincidofovir (200 mg once weekly orally) and all three experienced increased liver enzymes, necessitating the cessation of treatment.¹

Clinicians who request and acquire an FDA-approved single-patient emergency use IND (e-IND) are permitted to access brincidofovir from the SNS for the treatment of monkeypox. People with positive test findings for the human monkeypox virus who have severe disease or are at high risk for progression to severe disease will be taken into consideration for the FDA's review criteria for brincidofovir e-IND requests for treating monkeypox infections in people.¹⁶

Vaccinia Immune Globulin Intravenous

FDA has granted Vaccinia Immune Globulin Intravenous (VIGIV) a licence to be used in the management of vaccinia vaccination-related side effects. However, treating monkeypox with it is not permitted. As a result, the CDC has an expanded access IND protocol that permits the use of pre-stocked VIGIV for the treatment of orthopoxviruses, including monkeypox, during an outbreak. There are no accessible data on the effectiveness of VIGIV in treating human infections with the monkeypox virus. It is uncertain whether VIGIV therapy will help a patient with a severe monkeypox infection. However, medical professionals may consider its use in serious conditions when the production of a strong antibody response may be inhibited. VIGIV can be used as a preventative measure in exposed individuals with significant immunodeficiency in T-cell function when smallpox or monkeypox vaccination is not recommended. The United States Government does not have VIGIV prepositioned. On a case-by-case basis, CDC will provide it upon clinician request.^{16,34}

Vaccine for monkeypox

Mass immunisation cannot be possible for healthy person in this monkey epidemics. First-generation vaccines are smallpox vaccines created and effectively used at the intensive smallpox eradication program (SEP) in contrast to smallpox vaccines created after the end of the eradication phase or subsequently and made using modern cell culture method. Second-generation vaccines are smallpox vaccines produced using the same strain of vaccinia virus that is used in

Table 2. WHO Vaccine choice for monkeypox per 24 August 2022³⁵

Vaccine	Manufacture	Licensed country for monkeypox vaccine	consideration	Presentation	Injection materials
JYNNEOS® (MVA-BN) Vaccine- Third generation	Bavarian Nordic	Full market authorization (2019) in USA (JYNNEOS®) Europe (IMVANEX®) and Canada (IMVAMUNE®) under exceptional circumstances (2022)	Two doses spaced 28 days (4 weeks) apart is approved for general adult population. USA has granted emergency authorization for usage to people under the age of 18 (August 2022). Single-dose administration is approved for usage in both adults and infants and children of all ages.	A single dose or possibly multiple dose vials of liquid frozen or freeze-dried (lyophilized) vaccine	Subcutaneous administration through needle and syringe
LC16 KMB (LC16m8) Third generation	KM Biologics	Marketing authorization in Japan (2022)		Multidose vials of freeze-dried vaccine	Bifurcated needle
ACAM2000-Second generation	Emergent BioSolutions	US FDA Emergency Investigational new drug (EIND) program for the PEPE	Approved as a single dose in person between 18-64 years age.	multidose vials of freeze-dried vaccine	Bifurcated needle

first-generation vaccines, or clonal virus variations plaque-purified from conventional vaccine supplies and produced on specified cell lines. Third-generation vaccinations are those that have undergone additional passages in cell culture or animals, and were especially created as safer vaccines like LC16 and MVA-BN towards or after the eradication phase conclusion.³⁵

Three vaccinations, MVA-BN, LC16, or ACAM2000 can be taken into consideration for approved or off-label indication for the prophylaxis (pre and post-exposure) of monkeypox. Two of these vaccines, MVA-BN and LC16, have received approval for the purpose of preventing monkeypox. However, only the persons who are at risk and has had close contact with monkeypox infected patient should get the vaccine. At present, widespread immunisation is not possible.³⁶ The live vaccinia virus in vaccines that are slightly replicating (like LC16 from KM Biologics) and nonreplicating (like MVA-BN from Bavarian Nordic) has been greatly attenuated and has improved safety profiles. These vaccines produce antibodies against orthopoxviruses.³⁶

Newer and safer vaccines that have been created for the smallpox, which has been eradicated. may potentially be beneficial for monkeypox. Smallpox vaccine has been shown to be protective against monkeypox in the past. However, currently, no clinical information is available on the effectiveness of modern vaccines for smallpox/monkeypox.⁴

The need-risk-benefit analysis for vaccine selection should consider the safety, reactogenicity, and risk of vaccination-related adverse events. Replicating vaccinia-based vaccinations (like ACAM2000 or other vaccines created using cell culture method), minimally replicating vaccines (like LC16), or non-replicating vaccines (like MVA-BN) may be considered for healthy people. A particular non-replicating monkeypox vaccine like MVA-BN would be chosen for people for whom a regular replicating vaccination (such as ACAM2000) is contraindicated due to immunological deficiencies, immunosuppressive therapy, or atopic dermatitis. When pre-or post-exposure vaccination is being considered for women during pregnancy or breastfeeding, MVA-BN, a non-replicating or LC16, a minimally replicating vaccines are preferable. If vaccination

for post-exposure prophylaxis is being considered for children, non-replicating (MVA-BN) or minimally replicating (LC16) vaccines are preferred.³⁶ LC16 and MVA have received emergency use permission for children in Japan, and USA, respectively.³⁵

The vaccines currently on the market for monkeypox are listed in Table 2, along with their regulatory status. In order to prevent disease onset or lessen its adverse effects, persons in close contact with infected patients are advised to get post-exposure preventive vaccination (PEPV) with second or third-generation vaccine, within four days of first contact (and within 14 days if no symptoms appear). As suitable and accessible, PEPV can be given along with any of the vaccinations indicated in Table 2. The timing of vaccinations varies per product.

JYNNEOS® (MVA-BN) Vaccine

JYNNEOS (MVA-BN) is an authorised vaccine to prevent both smallpox and monkeypox. It is the main vaccination being used to combat the monkeypox outbreak. MVA-BN® (Modified Vaccinia Ankara - Bavarian Nordic) is a patented and exclusive vaccination platform technology of Bavarian Nordic.³⁷ An attenuated (weaker) form of the vaccine virus is known as modified vaccinia Ankara (MVA). It is used as a vaccination against smallpox and monkeypox and is known as MVA-BN. The two-dose MVA-BN (JYNNEOS®, USA; IMVANEX®, Europe; IMVAMUNE®, Canada) was authorised by the European Medicines Agency EMEA/H/C/002596 in 2013 and the U.S. Food and Drug Administration (FDA) on September 24, 2019. It is now indicated for preventing smallpox and monkeypox (MPXV) diseases in adults who have been found to be at high risk for infection. Its brand names are IMVANEX® in the Europe, IMVAMUNE®, in Canada, and JYNNEOS®, in the US. It has less adverse effects than the conventional smallpox vaccine. Based on this live, attenuated vaccinia virus (MVA), MVA-BN vaccine can induce a strong immune response even though it cannot replicate in the human body.³⁸ The JYNNEOS (MVA-BN) vaccine is cultured using chicken embryo fibroblast cells and a media devoid of serum. There are several processes used to purify and filter it out of the cells, including benzonase digestion. The Jynneos vaccination is not offered for purchase in the United States as

of November 2022.³⁸⁻⁴⁰ Regarding the effectiveness of the vaccine, recent studies have shown that MVA-BN stimulated a response even in people who already had immunity to vaccinia. This response included high cellular activity and a humoral (antibody) immune response about ten days after the second dose. On November 22, 2022, the UK Health Security Agency released its prediction of vaccine effectiveness for a single dosage at 78% 14 or more days following immunisation.⁴

The JYNNEOS vaccination is approved for two doses spaced 28 days (4 weeks) apart. The Jynneos vaccination can be given intradermally, in a layer extremely close to the surface of your skin, or subcutaneously, in the fat beneath your skin. The FDA-approved dosage regimen is the accepted protocol. In the standard regimen of subcutaneous (Subcut) form of administration, a 0.5mL injection volume is administered. The standard regimen has also been approved for people <18 years since August 9, 2022, under an Emergency Use Authorization. The vaccine is administered subcutaneously by injecting it into the fatty tissue, commonly over the triceps in children and adults older than 12 months of age or in the anterolateral thigh in infants and toddlers less than 12 months.

Under the terms of an Emergency Use Authorization that was given on August 9, 2022, an alternative regimen may be utilised in the context of the current national Public Health Emergency (PHE) for individuals age > 18 years. A 0.1mL injection volume is administered through the intradermal (ID) route of administration as a permitted alternative regimen. An intradermal vaccine recipient should manifest "a visible pale elevation of the skin" known as a wheal.

A clinical study's findings demonstrated that the lower intradermal dose was immunologically equivalent to the regular subcutaneous dose.⁴¹ MPOX vaccinations can protect person from the disease, but not right away. The maximum level of protection against MPOX is provided by receiving two doses of Jynneos. Approximately two weeks after receiving their second JYNNEOS shot, a person is deemed fully protected.³⁸

JYNNEOS may often be given without consideration to the time of most other vaccines because it is based on live, attenuated, non-

replicating orthopoxvirus. This covers the concurrent administration of JYNNEOS and other vaccines, such as the influenza shot, but at different body site. When giving the COVID-19 vaccination, there are additional factors to consider. (Interim Clinical Guidelines for the Administration of COVID-19 Vaccines). There is no requirement that patients who have previously had the received COVID-19 vaccine wait a certain amount of time before receiving the orthopoxvirus vaccine (either JYNNEOS or ACAM2000). The Jynneos vaccine will be accessible to most HIV-positive patients.⁴

ACAM2000

ACAM2000 is a replication-competent smallpox vaccine that can be given to only a few people. Emergent BioSolutions currently manufactures the ACAM2000 vaccine. ACAM2000 vaccine includes the contagious Vaccinia virus, a live virus that can infect other persons. The vaccinia virus is of same virus family as that small or monkeypox viruses therefore, it can be used in protecting humans from monkeypox infection. ACAM2000 has a higher rate of side effects than the MVA vaccination. It has been given approval in the US to prevent smallpox. A CDC-approved expanded-access investigational new drug (EA-IND) application approve its usage in treating monkeypox. It is an alternative to the JYNNEOS vaccine.^{1,4,36,42,43} ACAM2000 effect against monkeypox is uncertain, but one study suggested that its precursor Dryvax, smallpox vaccine (the first-generation), showed protection against monkeypox among 1555 vaccinated contacts of 338 patients in the Democratic Republic of the Congo (then known as Zaire).⁴⁴ The evidence for immunogenicity is moderate.⁴⁵ ACAM2000 is derived from a clone of the previously used vaccine "Dryvax." Like the previous "Dryvax" vaccine, ACAM2000 should not be given to individuals who are immunocompromised or pregnant since it can induce pericarditis and myocarditis. The ACAM2000 is the first vaccination to have a medication guide approved by the U.S. Food and Drug Administration, with a screening protocol prior to injection.⁴⁶ For individuals aged 1 and older who have been shown to be at high risk for infection, the CDC suggests that immunisation with ACAM2000 can be taken into consideration to prevent monkeypox. It is recommended to

administer the ACAM2000 vaccination in a single dose by repeatedly pricking the skin, often on the upper arm. Individuals are deemed to be fully protected after four weeks of getting ACAM2000. Simultaneous immunization is not advisable after getting the ACAM2000 vaccine. If a person receives the ACAM2000 vaccination, a live injectable vaccine such as the MMR or varicella vaccine (chickenpox) should not be given on the same day. There should be at least 28 days between them and the COVID-19 injections may be postponed by 4 weeks.⁴

LC16 KMB

LC-16 is a third-generation live attenuated vaccine against minimally replication-competent vaccinia virus (LC16m8 strain) approved in Japan.¹ LC16 KMB (LC16m8) was developed by the Japanese company KM Biologics as a smallpox and monkeypox freeze-dried cell culture vaccine. KM Biologics (SVRG Kaketsuken) is a unit of Meiji Holdings, a Japanese food, and pharmaceuticals corporation with headquarters in Kumamoto, Japan. It was approved for use in Japan in 1975 for people of all ages and was granted a licence in the United States under the emergency investigational new drug programme. The government of Japan has not offered smallpox immunisation to the public since 1976. On August 2, 2022,⁴⁷ LC-16KMB was authorised by the Ministry of Health, Labour, and Welfare (MHLW) of Japan for pre-exposure prophylaxis (PrEP) for the monkeypox virus. After assessment by the advisory committee, this consent was given. A notification of additional approval of the indication for "Monkeypox Prevention for "LC16 KMB" was made public by Meiji Holdings on August 3, 2022. The National Agency of Drug and Food Control in Indonesia is examining authorisation as of August 31, 2022.⁴⁸

A 2017⁴⁹ study found that LC16m8 vaccination of people produced neutralising antibodies against smallpox virus, and the impact was same to that of the ACAM2000 smallpox vaccine.

The Lister vaccinia smallpox vaccine, designated LC16m8, was modified for cell culture attenuation and lacked the B5R protein. LC16m8 preserves most of the vaccinia genome in contrast to replication-deficient vaccines like Modified Vaccinia Ankara. Therefore vaccination recipients

may develop a "take lesion" due to its replication at the inoculation site.^{1,36,50} An immunosuppressed person, who suffers from atopic dermatitis, is pregnant, or has had an adverse reaction to any vaccine component should take the LC16 vaccine with caution. Administrators of the vaccine and healthcare professionals must be equipped to handle any anaphylactic reaction that may occur after LC16 administration. Following the administration of the LC1618 vaccine, patients may have mild side effects such as lymphadenopathy, fatigue, joint pain, rash, erythema at the inoculation site, fever, swelling at the inoculation site, and autoinoculation. Compared to those who received a booster shot, primary vaccination recipients experience far more side effects. There have been no recorded severe adverse effects. The conventional scarification technique is used to deliver LC16m8 in a single dosage. The strong store stability of LC16m8 was proven by its long-term storage stability for formulation i.e., 10 years and for drug substance i.e., 5 years.^{36,50}

Prevention against monkeypox

The danger of monkeypox transmission in public places and healthcare facilities can be reduced by implementing infection prevention and control strategies. Vaccination is one such important strategy. It requires a few weeks to develop immunity after getting vaccine, and it is not known yet that how well the vaccines provide protection to the person or if vaccine prevent persons from spreading infection to others because their monkeypox efficacy data is limited. However, considering the present vaccine shortage, individuals must temporarily alter some habits that can make them more susceptible to infection. Until there is an adequate supply of vaccines, this short-term precaution will help in slowing the monkeypox spread. It is crucial that between the first and second dose the activities that put people at risk of contracting monkeypox between the first and second doses of the vaccine. The highest protection is achieved two weeks following the second vaccination dosage.¹⁰

A person infected from monkeypox should avoid kissing, touching or vaginal, oral or anal intercourse to protect yourself and others if you or a partner has monkeypox or suspects they may have it. Avoid handling any rash in particular.

Habit of sharing thing of infected persons like towel, toothbrushes, sex toys and other personnel things should be discontinued. Monkeypox virus has been found in semen but the spreading of monkeypox virus through semen or vaginal secretion is still not known.

Person of any gender or sexual orientation, can develop MPOX. The most vulnerable are those who engage in sexual activity with numerous or new partners. Cisgender guys who have intercourse with men and their sex partners are particularly affected. Although there is little information available, anyone who might be involved in queer sexual networks should be aware of the effects of MPOX on trans and non-binary individuals.⁵¹

CONCLUSION

Monkeypox is a viral disease that spreads through close contact with an infected person. At present, no specific treatment is available for monkeypox. The treatment available for smallpox is considered for the management of monkeypox. Vaccines are not available for mass immunization. There is an urgent requirement to develop a specific treatment to combat this disease.

ACKNOWLEDGMENTS

None.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHOR'S CONTRIBUTION

Both the authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

FUNDING

None

DATA AVAILABILITY

All datasets generated or analyzed during this study are included in the manuscript.

ETHICS STATEMENT

Not applicable.

REFERENCES

- Adler H, Gould S, Hine P, et al. Clinical features and management of human monkeypox: a retrospective observational study in the UK. *Lancet Infect Dis*. 2022;22(8):1153-1162. doi: 10.1016/S1473-3099(22)00228-6
- Actor JK. Clinical Virology. *Elsevier's Integr Rev Immunol Microbiol*. 2012:129-138. doi: 10.1016/B978-0-323-07447-6.00014-4
- Abdelaal A, Serhan HA, Mahmoud MA, Rodriguez-Morales AJ, Sah R. Ophthalmic manifestations of monkeypox virus. *Eye*. 2022;7-10. doi: 10.1038/s41433-022-02195-z
- WHO. Monkeypox. Accessed November 23, 2022 https://www.who.int/news-room/questions-and-answers/item/monkeypox?gclid=Cj0KCQiAg_KbBhDLARIsANx7wAx62Is1Ji79ybYYBkylGMgdbKej3VslOWLueLlr0UciSN1N_TnD0DkaAgazEALw_wcB
- Sah R, Mohanty A, Siddiq A, et al. Monkeypox reported in India – South East Asia Region: Health and economic challenges. *Lancet Reg Heal - Southeast Asia*. 2022;4:100063. doi: 10.1016/j.lansea.2022.100063
- Yinka-Ogunleye A, Aruna O, Dalhat M, et al. Outbreak of human monkeypox in Nigeria in 2017–18: a clinical and epidemiological report. *Lancet Infect Dis*. 2019;19(8):872-879. doi: 10.1016/S1473-3099(19)30294-4
- Soheili M, Nasserli S, Afraie M, et al. Monkeypox: Virology, Pathophysiology, Clinical Characteristics, Epidemiology, Vaccines, Diagnosis, and Treatments. *J Pharm Pharm Sci*. 2022;25:297-322. doi: 10.18433/jpps33138
- Yong SEF, Ng OT, Ho ZJM, et al. Imported monkeypox, Singapore. *Emerg Infect Dis*. 2020;26(8):1826-1830. doi: 10.3201/eid2608.191387
- Rao AK, Schulte J, Chen T-H, et al. Monkeypox in a Traveler Returning from Nigeria - Dallas, Texas, July 2021. *MMWR Morb Mortal Wkly Rep*. 2022;71(14):509-516. doi: 10.15585/MMWR.MM7114A1
- Isaacs ASN, Shenoy ES, Goldfarb IT. Treatment and prevention of monkeypox - UpToDate. UpToDate. 2022:1-33. [https://www.uptodate.com.ezproxy.uninorte.edu.co/contents/treatment-and-prevention-of-monkeypox?search=viruela simica&source=search_result&selectedTitle=1~39&usage_type=default&display_rank=1](https://www.uptodate.com.ezproxy.uninorte.edu.co/contents/treatment-and-prevention-of-monkeypox?search=viruela%20simica&source=search_result&selectedTitle=1~39&usage_type=default&display_rank=1)
- Abdi SAH, Ali A, Sayed SF, Abutahir, Ali A, Alam P. Multi-Epitope-Based Vaccine Candidate for Monkeypox: An In Silico Approach. *Vaccines*. 2022;10(9):1-13. doi: 10.3390/vaccines10091564
- Sherwat A, Brooks JT, Birnkrant D, Kim P. Tecovirimat and the Treatment of Monkeypox - Past, Present, and Future Considerations. *N Engl J Med*. 2022;387(7):579-581. doi: 10.1056/NEJMP2210125
- Rizk JG, Lippi G, Henry BM, Forthal DN, Rizk Y. Prevention and Treatment of Monkeypox. *Drugs*. 2022;82(9):957-963. doi: 10.1007/s40265-022-01742-y
- fda, Cder. FULL PRESCRIBING INFORMATION TPOXX[®]. United States Food and Drug Administration (FDA) Accessed November 29, 2022. www.fda.gov/medwatch
- STOMP: Study of Tecovirimat for Human Monkeypox Virus. STOMP. Accessed November 29, 2022. <https://www.stomptpox.org/main>
- CDC. Monkeypox Treatment Information for Healthcare Professionals Interim Clinical Guidance for the Treatment of Monkeypox Medical Countermeasures Available for the Treatment of Monkeypox. United States Centers for Disease Control and Prevention.
- Russo AT, Grosenbach DW, Brasel TL, et al. Effects of treatment delay on efficacy of tecovirimat following lethal aerosol monkeypox virus challenge in cynomolgus macaques. *J Infect Dis*. 2018;218(9):1490-1499. doi: 10.1093/infdis/jiy326
- Russo AT, Berhanu A, Bigger CB, et al. Co-administration of tecovirimat and ACAM2000TM in non-human primates: Effect of tecovirimat treatment on ACAM2000 immunogenicity and efficacy versus lethal monkeypox virus challenge. *Vaccine*. 2020;38(3):644-654. doi: 10.1016/j.vaccine.2019.10.049
- Berhanu A, Prigge JT, Silvera PM, Honeychurch KM, Hruby DE, Grosenbach DW. Treatment with the smallpox antiviral tecovirimat (ST-246) alone or in combination with ACAM2000 vaccination is effective as a postsymptomatic therapy for monkeypox virus infection. *Antimicrob Agents Chemother*. 2015;59(7):4296-4300. doi: 10.1128/AAC.00208-15
- Desai AN, Thompson GR, Neumeister SM, Arutyunova AM, Trigg K, Cohen SH. Compassionate Use of Tecovirimat for the Treatment of Monkeypox Infection. *JAMA*. 2022;328(13):1348-1350. doi: 10.1001/jama.2022.15336
- Hernandez LE, Jadoo A, Kirsner RS. Human monkeypox virus infection in an immunocompromised man: trial with tecovirimat. *Lancet*. 2022;400(10355):e8. doi: 10.1016/S0140-6736(22)01528-8
- Study of Tecovirimat for Human Monkeypox Virus. Accessed November 29, 2022. <https://clinicaltrials.gov/ct2/show/NCT0534984>
- Smith JA, Casey CG, Tierney BC, Semba RD. The ocular complications of smallpox and smallpox immunization. *Arch Ophthalmol*. 2004;122(9):1407-1408. doi: 10.1001/archophth.122.9.1407-a
- O'Laughlin K, Tobolowsky FA, Elmor R, et al. Clinical Use of Tecovirimat (TPOXX) for Treatment of Monkeypox Under an Investigational New Drug Protocol - United States, May-August 2022. *MMWR Morb Mortal Wkly Rep*. 2022;71(37):1190-1195. doi: 10.15585/MMWR.MM7137E1
- Grosenbach DW, Honeychurch K, Rose EA, et al. Oral Tecovirimat for the Treatment of Smallpox. *N Engl J Med*. 2018;379(1):44-53. doi: 10.1056/NEJMOA1705688/SUPPL_FILE/NEJMOA1705688_DISCLOSURES.PDF
- U.S. clinical trial evaluating antiviral for monkeypox begins. Accessed November 28, 2022. National Institutes of Health (NIH). <https://www.nih.gov/news-events/news-releases/us-clinical-trial-evaluating-antiviral-monkeypox-begins>
- Stittelaar KJ, Neyts J, Naesens L, et al. Antiviral treatment is more effective than smallpox vaccination

- upon lethal monkeypox virus infection. *Nature*. 2006;439(7077):745-748. doi: 10.1038/NATURE04295
28. Smee DF. Progress in the discovery of compounds inhibiting orthopoxviruses in animal models. *Antivir Chem Chemother*. 2008;19(3):115-124. doi: 10.1177/095632020801900302
 29. Baker RO, Bray M, Huggins JW. Potential antiviral therapeutics for smallpox, monkeypox and other orthopoxvirus infections. *Antiviral Res*. 2003;57(1-2):13-23. doi: 10.1016/S0166-3542(02)00196-1
 30. FDA approves drug to treat smallpox, FDA. Accessed November 29, 2022. <https://www.fda.gov/drugs/news-events-human-drugs/fda-approves-drug-treat-smallpox>.
 31. Parker S, Chen NG, Foster S, et al. Evaluation of disease and viral biomarkers as triggers for therapeutic intervention in respiratory mousepox - an animal model of smallpox. *Antiviral Res*. 2012;94(1):44-53. doi: 10.1016/J.ANTIVIRAL.2012.02.005
 32. Hutson CL, Kondas A V., Mauldin MR, et al. Pharmacokinetics and Efficacy of a Potential Smallpox Therapeutic, Brincidofovir, in a Lethal Monkeypox Virus Animal Model. *mSphere*. 2021;6(1). doi: 10.1128/MSPHERE.00927-20
 33. Rice AD, Adams MM, Wallace G, et al. Efficacy of CMX001 as a post exposure antiviral in New Zealand White rabbits infected with rabbitpox virus, a model for orthopoxvirus infections of humans. *Viruses*. 2011;3(1):47-62. doi: 10.3390/V3010047
 34. Centers for Disease Control and Prevention. Expanded Access IND Protocol: Use of Tecovirimat (TPOXX[®]) for Treatment of Human Non-Variola Orthopoxvirus Infections in Adults and Children. 2022;(10788). <https://www.cdc.gov/poxvirus/monkeypox/pdf/Tecovirimat-IND-Protocol-CDC-IRB.pdf>
 35. World Health Organization. Vaccines and Immunization for Monkeypox: Interim Guidance, 24 August 2022.; 2022. <https://www.who.int/publications/i/item/who-mpx-immunization-2022.1>
 36. WHO. Vaccines and immunization for monkeypox. *Who*. 2022;(June):1-28. <https://www.who.int/publications/i/item/who-mpx-immunization-2022.1>
 37. MVA-BN. MVA-BN. Bavarian Nordic. Accessed November 25, 2022. <https://www.bavarian-nordic.com/pipeline/technology/mva-bn.aspx>
 38. Center for Disease Control and Prevention. *JYNNEOS Vaccine*. 2022:22-23. <https://www.cdc.gov/poxvirus/monkeypox/interim-considerations/jynneos-vaccine.html>
 39. Monkeypox S, Description V. JYNNEOS Smallpox (Monkeypox) Vaccine JYNNEOS[®] (MVA-BN) Smallpox Monkeypox Vaccine Description 2022. 2022;19:1-27.
 40. Ilchmann H, Samy N, Reichhardt D, et al. Single and 2-dose vaccinations with modified vaccinia Ankara-Bavarian Nordic[®] induce durable B cell memory responses comparable to replicating smallpox vaccines. *J Infect Dis*. 2022. doi: 10.1093/INFDIS/JIAC455
 41. Frey SE, Wald A, Edupuganti S, et al. Comparison of lyophilized versus liquid modified vaccinia Ankara (MVA) formulations and subcutaneous versus intradermal routes of administration in healthy vaccinia-naïve subjects. *Vaccine*. 2015;33(39):5225-5234. doi: 10.1016/J.VACCINE.2015.06.075
 42. CDC. ACAM2000 Vaccine. Accessed November 23, 2022. <https://www.cdc.gov/poxvirus/monkeypox/vaccines/acam2000.html>
 43. JYNNEOS C. Interim Clinical Considerations for Use of JYNNEOS and ACAM2000 Vaccines during the 2022 U.S. Monkeypox Outbreak. Monkeypox. Poxvirus. CDC. Accessed November 23, 2022. https://www.cdc.gov/poxvirus/monkeypox/clinicians/vaccines/vaccine-considerations.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fpoxvirus%2Fmonkeypox%2Fhealth-departments%2Fvaccine-considerations.html
 44. Jeiek Z, Grab B, Szczeniowski M V, Palju KM, Mutombo M. Human monkeypox: secondary attack rates. *Bull World Health Organ*. 1988;66(4):465-470.
 45. Petersen BW, Harms TJ, Reynolds MG, Harrison LH. Use of Vaccinia Virus Smallpox Vaccine in Laboratory and Health Care Personnel at Risk for Occupational Exposure to Orthopoxviruses — Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2015. *MMWR Morb Mortal Wkly Rep*. 2019;65(10):257-262. doi: 10.15585/MMWR.MM6510A2
 46. Mullendore NF, Lawner BJ, Malone JD. Monkeypox attack. In: Ciottoni's Disaster Medicine. *Elsevier Inc*. 2016:774-776. doi: 10.1016/B978-0-323-28665-7.00149-7
 47. JIHO I. Japan Approves KM Biologics' Smallpox Vaccine for Monkeypox. Pharma Japan. Accessed November 26, 2022. <https://pj.jiho.jp/article/247203>
 48. Risalah DF. Bio Farma Reveals Three Candidates for Monkey Pox Vaccine to be Used in Indonesia. *REPUBLIKA.CO.ID*. 2022:1-7.
 49. Saijo M. Research on the efficacy, safety, and productivity improvement of the cell-cultured smallpox vaccine developed and stockpiled in Japan, and on the ideal countermeasures against bioterrorism in Japan and overseas. Ministry of Health, Labor and Welfare (MHLW) Ministry of Health, Labor and Welfare research. 2019. Accessed November 26, 2022. <https://research-er.jp/projects/view/1044205>
 50. LC16 KMB (LC16m8) Monkeypox (Smallpox) Vaccine — Precision Vaccinations. <https://www.precisionvaccinations.com/vaccines/lc16-kmb-lc16m8-monkeypox-smallpox-vaccine>. Accessed November 23, 2022.
 51. CDC. Monkeypox and Safer Sex. Accessed November 26, 2022. <https://www.cdc.gov/poxvirus/monkeypox/prevention/sexual-health.html>