



Clinical Considerations for Treatment and Prophylaxis of Monkeypox Virus Infection in People with HIV

Updated August 17, 2022

Summary of Changes

Updates as of August 8, 2022

- Updated tecovirimat considerations for people with HIV

Who this is for: Healthcare professionals providing care for people with HIV.

What this is for: Considerations for the care of people with HIV, including prevention and treatment of monkeypox.

How to use: This information is intended as an aid for staff at healthcare facilities and healthcare professionals developing plans for monkeypox treatment and prophylaxis for people with HIV.

Key Points

- People with advanced HIV or who are not virologically suppressed with antiretroviral therapy can be at increased risk of severe disease with monkeypox.
- Post-exposure prophylaxis and antiviral treatments are available for people exposed to monkeypox or with monkeypox virus infection. Vaccination with JYNNEOS is considered safe for people with HIV, and antiviral treatments for monkeypox have few interactions with antiretroviral therapy.

These considerations are based upon limited evidence available to date about monkeypox in people with HIV. The approaches outlined below are intentionally cautious until additional data become available.

Monkeypox in People with HIV

Available summary surveillance data from the European Union^{1,2,3}, England⁴, and the United States⁵ indicate that among gay, bisexual, and other men who have sex with men (MSM) with monkeypox for whom HIV status is known, 28%–51% have HIV infection.

Regarding infection risk, it is currently unknown whether an HIV infection alters (e.g., increases) a person's risk of acquiring monkeypox disease after exposure.

Regarding illness after infection, the available data indicate that people with advanced and uncontrolled HIV can be at a higher risk of severe or prolonged monkeypox disease. In a 2017–18 case series of 122 Nigerian patients with monkeypox, 4 of the 7 deaths occurred among people with untreated advanced HIV; however, information was absent about the overall proportion of patients who had HIV to determine if this mortality was disproportionately large.⁶ A second 2017–18 case series, also from Nigeria, included 9 people with HIV for whom clinical data relevant to HIV status were provided: CD4 cell counts ranged from 20–357 cells/mm³ and most had either failed antiretroviral therapy (ART) or were newly diagnosed, suggesting a

lack of viral suppression. Compared with other patients, those with HIV had higher rates of secondary bacterial infection, more prolonged illness (and thereby also longer period of infectiousness), as well as a greater likelihood of a confluent or partially confluent rash rather than discrete lesions.⁷ In contrast, reports from European countries where most patients are on effective ART have noted no deaths or evident excess in hospitalizations thus far among people with HIV and monkeypox.²⁻⁴ Additionally, the WHO has stated that “people with HIV...who take antiretroviral therapy and have a robust immune system have not reported a more severe course of disease.”⁸

Signs and Symptoms

The [signs and symptoms](#) of monkeypox virus infection are similar in people with or without HIV, including characteristic rash, fever, and lymphadenopathy. For immunocompromised people, monkeypox virus infection may present with atypical manifestations or more severe illness (e.g., sepsis, disseminated rash).

Monkeypox disease is characterized by an incubation period, prodrome, and rash. For full details, please see [Clinical Recognition | Monkeypox | Poxvirus | CDC](#).

Incubation and prodrome

It is not known if people with HIV have different characteristics regarding the incubation or prodromal phase of illness.

Illness

Immunocompromised people, including people with advanced HIV or untreated HIV, may present with an atypical rash, including a disseminated rash, which may make diagnosis more challenging. In one study, people with poorly controlled HIV were more likely to have genital lesions and a confluent or partially confluent rash, as opposed to discrete lesions.⁶ Additionally, people in this study with poorly controlled HIV were more likely to have prolonged illness.

Differential diagnosis

Monkeypox virus infection should also be considered when evaluating for other causes of rash, including herpes zoster (shingles), scabies, molluscum contagiosum, herpes, syphilis, chancroid, lymphogranuloma venereum, allergic skin rashes, and drug eruptions. Monkeypox can be confused with disseminated herpes zoster or herpes simplex virus infections. These herpesvirus infections more commonly affect people with immunocompromising conditions, especially disseminated herpes zoster. Therefore, to establish a diagnosis for immunocompromised people who present with a rash, clinicians should conduct a thorough history to assess for possible monkeypox exposures or epidemiologic risk factors, perform a complete physical examination, and order lab testing. Co-infections with monkeypox and sexually transmitted infections (STI) have been reported, therefore a broad approach to testing is recommended, including STI testing.⁹

For additional recommendations regarding case finding and clinical presentation, please see: [Updated Case-finding Guidance: Monkeypox Outbreak—United States, 2022](#)

For additional recommendations on specimen collection for clinicians, please see: [Preparation and Collection of Specimens | Monkeypox | Poxivirs | CDC](#)

Treatment

Managing monkeypox in people with HIV

People with HIV may be at increased risk of severe disease and prolonged infectiousness. Therefore, prophylaxis (e.g., vaccination), [medical treatment](#) and close [monitoring](#) are a priority for this population. Providers should consider both viral suppression and CD4 count in weighing the risk of severe outcomes for any patient with HIV. As noted earlier, severe outcomes have been observed in people with inadequately treated HIV who have CD4 counts $\leq 350/\text{mm}^3$ and are likely not virologically suppressed; however, the available data are presently insufficient to define actionable thresholds. Until more is known, clinicians should exercise clinical judgement to assess the extent of immunosuppression (from HIV or any other source) and the risk for severe monkeypox illness. The patient's clinical team is best positioned to determine the degree of

sources) and the risk for severe monkeypox illness. The patient's clinical team is best positioned to determine the degree of immune compromise and, with the input of public health practitioners, the need for prophylaxis (including vaccination) and treatment. The decision to treat and monitor an immunocompromised person in their home or an inpatient setting should likewise be individualized.

Managing HIV in people with monkeypox

ART and opportunistic infection prophylaxis should be continued in all people with HIV who develop monkeypox. Treatment interruption may lead to rebound viremia that could complicate the management of monkeypox virus infection (e.g., worsen the severity of illness). People taking antiretrovirals for HIV pre-exposure prophylaxis (PrEP) or post-exposure prophylaxis (PEP) should likewise continue taking these medications.

For people with HIV diagnosed coincident with monkeypox or who are not taking ART, [CDC recommends](#) starting ART as soon as possible, and in consultation with an expert in HIV medicine if needed.

Clinicians using antivirals for monkeypox need to be alert for drug-drug interactions with any antiretrovirals used to treat¹⁰ or prevent^{11, 12} HIV infection as well as with any other medications used to prevent or treat HIV-related opportunistic infections.¹³ Key critical interactions are discussed below for each monkeypox antiviral. Any potential drug-drug interactions not noted below can be assessed using the University of Liverpool HIV Drug Interactions database, an interactive online tool found at: <https://www.hiv-druginteractions.org/checker> [↗](#).

Treatment options

Tecovirimat (a.k.a. TPOXX, ST-246)

Tecovirimat is an antiviral medication available as a pill or as an injection for intravenous (IV) administration. It is approved by the FDA for treatment of smallpox in adults and children but not for monkeypox because data are not available on the effectiveness of tecovirimat in treating monkeypox in humans.

Tecovirimat can be administered under an expanded access Investigational New Drug ([EA-IND](#)) protocol and is available from the Strategic National Stockpile (SNS).

Studies using a variety of animal species have shown that tecovirimat is effective in treating orthopoxvirus-induced disease.¹⁴ Human clinical trials indicated the drug was safe and tolerable with only minor side effects.¹⁵ A case report from the UK suggested that tecovirimat may shorten the duration of illness and viral shedding.¹⁶

Cidofovir and Brincidofovir

Cidofovir is approved by the FDA for treatment of cytomegalovirus (CMV) retinitis in patients with advanced HIV. It is administered as an intravenous infusion. Brincidofovir is approved by the FDA for the treatment of human smallpox disease in adult and pediatric patients, including neonates. It is administered orally as a tablet or oral suspension. Currently, only cidofovir is available, either commercially or from the SNS.

Data are not available on the effectiveness of cidofovir and brincidofovir in treating human cases of monkeypox. However, both have proven activity against poxviruses in *in vitro* and animal studies. At this time, it is unknown if a person with severe monkeypox virus infection will benefit from treatment with either antiviral, although their use may be considered in such instances.

Vaccinia Immune Globulin Intravenous (VIGIV)

Data are not available on the effectiveness of VIGIV in treatment of monkeypox virus infection. VIGIV for the treatment of monkeypox is administered under an EA-IND, and it is unknown whether a person with severe monkeypox virus infection will benefit from treatment with VIGIV. However, healthcare providers may consider its use in severe cases.

For further details regarding therapeutic recommendations and clinical guidance for the treatment on monkeypox, see [Treatment](#) and [Clinician FAQs](#).

Considerations for use in people with HIV

Tecovirimat (a.k.a. TPOXX, ST-246)

Few interactions are expected with antiretroviral therapy for HIV. However, none of the identified drug interactions should preclude coadministration of tecovirimat and antiretroviral therapy. According to the [Liverpool HIV drug interactions database](#) [↗](#), tecovirimat may result in a reduction in levels of non-nucleoside reverse transcriptase inhibitors (NNRTIs) doravirine and rilpivirine, and the CCR5 antagonist maraviroc. Dose increases for doravirine, rilpivirine, and maraviroc could be considered when co-administered with tecovirimat and for two weeks after completion of tecovirimat therapy (see [Liverpool website](#) [↗](#) for details). However, based on evidence graded very low quality and the short treatment course of tecovirimat, some [experts](#) [↗](#) believe neither dose adjustments nor additional ART are needed. Consultation with local pharmacists is suggested.

When co-administering tecovirimat with long-acting cabotegravir/rilpivirine, tecovirimat might result in a reduction in rilpivirine levels. Per the [Liverpool HIV interactions database](#) [↗](#), the addition of oral rilpivirine 25mg once daily (or the patient's prior ART regimen) during treatment with tecovirimat and for approximately 2 weeks after the end of treatment could be considered. However, some experts believe no additional therapy is necessary during tecovirimat treatment. Initiation of long-acting cabotegravir/rilpivirine should be **avoided** [🚫](#) [↗](#) during tecovirimat therapy and for 2 weeks after the conclusion of tecovirimat.

Cidofovir and Brincidofovir

Cidofovir is contraindicated in patients with serum creatinine >1.5 mg/dL because of the nephrotoxicity associated with these medications. Therefore, co-administration of cidofovir with tenofovir disoproxil fumarate (TDF) is **not** recommended. If concomitant use of TDF and nephrotoxic agents is unavoidable, renal function should be monitored closely. Cidofovir is typically co-administered with probenecid both to reduce nephrotoxicity and boost its effectiveness. Probenecid substantially increases zidovudine plasma levels; if co-administered, zidovudine should either be temporarily discontinued or decreased by 50% on the day of cidofovir-probenecid administration to avoid zidovudine-induced hematological toxicity.

Brincidofovir has clinically relevant drug interaction with protease inhibitors (PIs), cobicistat, and fostemsavir that may require modification of therapy. If PIs or fostemsavir are co-administered with brincidofovir, clinicians should monitor closely for adverse reactions (e.g., elevations in transaminase levels) and dosing of antiretroviral therapy should be delayed for at least 3 hours after brincidofovir administration.

Both cidofovir and brincidofovir have interactions (including contraindications for use) with other medications that should be assessed by the clinical team. Currently, only cidofovir is available, either commercially or from the SNS.

Vaccinia Immune Globulin Intravenous (VIGIV)

There are no specific contraindications for use of VIGIV among people with HIV, and no known or anticipated interactions with antiretroviral therapy.

Monkeypox can cause keratitis. Caution should be exercised when using VIGIV in the treatment of people with active keratitis, as increased corneal scarring was observed in an animal model of vaccinia keratitis.

VIGIV is contraindicated in individuals with a history of anaphylaxis or prior severe systemic reaction association with the parenteral administration of this or other human immune globulin preparations. VIGIV is contraindicated in IgA-deficient patients with antibodies against IgA and a history of IgA hypersensitivity.

Vaccination with live virus vaccines (e.g., varicella, measles, mumps, and rubella) should be deferred for 3 months after use of VIGIV.

For additional details regarding therapeutic recommendations, see [Treatment](#).

Pre- and Post-Exposure Prophylaxis

Preexposure prophylaxis

Preexposure prophylaxis should be offered to people with HIV if [indicated](#). At this time, the only form of preexposure prophylaxis available or authorized for monkeypox is [vaccination](#). The risks and benefits of preexposure prophylaxis by vaccination should be discussed with the patient using shared decision-making.

When preexposure prophylaxis by vaccination is chosen, JYNNEOS should be used for people with HIV. Given limited supply of JYNNEOS vaccine, the national vaccine strategy for monkeypox is implementing a phased approach. During the initial phases, priority should be given to postexposure prophylaxis. In later phases, vaccine supply will increase and will make preexposure prophylaxis more feasible. Based on available guidance from ACIP, ACAM2000 should not be used for people with HIV due to the risk of adverse effects from the spread of vaccinia virus.

Postexposure prophylaxis


Postexposure prophylaxis by [vaccination](#) should be offered to people with HIV if indicated. The risks and benefits of postexposure prophylaxis by vaccination should be discussed with the patient using shared decision-making. Other therapies, including the antiviral medication tecovirimat and vaccinia immune globulin, may be considered for monkeypox PEP on an individual case-by-case basis depending on the known [high-risk exposure](#) to a confirmed or probable case of infection and clinical conditions that necessitate an alternative option to PEP vaccination. The efficacy of these therapies as monkeypox PEP is unknown.

While the use of smallpox vaccines for post-exposure prophylaxis has not been studied, early use of vaccination (within 4 days from exposure) could prevent monkeypox virus infection and later use (5 days or more after exposure) may decrease the severity of monkeypox disease if infection occurs.

When postexposure prophylaxis by vaccination is chosen, JYNNEOS should be used for people with HIV due to the risk of adverse effects from the spread of vaccinia virus.


Vaccine Safety and Efficacy

JYNNEOS

[JYNNEOS](#)  is a two-dose live virus vaccine that uses non-replicating modified vaccinia Ankara (MVA).^[17] It is licensed by FDA for prevention of both smallpox and monkeypox disease in adults 18 years of age and older. The safety and immunogenicity of JYNNEOS has been specifically evaluated in people with HIV. In one study, which enrolled people with HIV with CD4 counts between 200 and 750 cells/mm³, the rates of adverse events did not differ between people with and without HIV.^[18] In another study, which enrolled people with HIV and CD4 counts >350 cells/mm³ and people without HIV, vaccination was well tolerated and comparably immunogenic in terms of neutralizing antibody responses in both groups.^[19] In another trial specifically enrolling people with a prior diagnosis of AIDS who were virologically suppressed and had CD4 counts between 100 and 500, there were no serious safety concerns, and the vaccine appeared efficacious based on immunogenicity at standard dosing.^[20] Immunogenicity among people with HIV who have CD4 counts below 100 cells/mm³ or who are not virologically suppressed remains unknown.

For more information, please see: [Monkeypox and Smallpox Vaccine Guidance](#) and [Considerations for Monkeypox Vaccination | Monkeypox | Poxvirus | CDC](#).

ACAM2000

[ACAM2000](#)  is a single-dose live virus vaccine that uses replicating vaccinia. It is licensed by FDA for prevention of smallpox. ACAM2000 should not be given to people with HIV (regardless of immune status). Severe localized or systemic infection with vaccinia (progressive vaccinia) may occur in people with weakened immune systems, including from HIV.

ACAM2000 vaccination should also be avoided if the vaccine recipient cannot sufficiently isolate from household contacts who have a history of atopic dermatitis or other active exfoliative skin condition, an immunocompromising condition, or who are pregnant or aged <1 year. Household contacts include people with prolonged intimate contact with the potential vaccinee

(e.g., sexual contacts) and others who might have direct contact with the vaccination site or with potentially contaminated materials (e.g., clothing or vaccination site dressings).

For more information, please see: [Monkeypox and Smallpox Vaccine Guidance](#) and [Considerations for Monkeypox Vaccination | Monkeypox | Poxvirus | CDC](#).

Vaccine adverse events

All adverse reactions should be reported to the Vaccine Adverse Event Reporting System (VAERS). Reports can be filed by healthcare providers or by vaccine recipients. To file an adverse reaction report, please visit www.vaers.hhs.gov or call 1-800-822-7967. VAERS is only for reporting reactions, and VAERS staff members do not give medical advice.

U.S. healthcare providers and health department staff with a complex monkeypox vaccine safety question about a specific patient residing in the U.S. or vaccine safety issue can contact the [Clinical Immunization Safety Assessment \(CISA\) Project](#) at CISAeval@cdc.gov to request a case consultation. In case of an emergent clinical vaccine safety inquiry, healthcare providers and health department staff can call the CDC Emergency Operations Center (EOC) Watch Desk at (770)-488-7100.

Patient Guidance

Prevention

People with HIV should follow the same guidance as anyone else to protect themselves from monkeypox.

- Avoid direct contact with rashes, sores, or scabs on a person with monkeypox, including during intimate contact such as sex. We believe this is currently the most common way that monkeypox is spreading in the U.S.
- Avoid contact with objects, fabrics (e.g., clothing, bedding, or towels), and surfaces that have been used by someone with monkeypox.
- Avoid contact with respiratory secretions, through kissing and other face-to-face contact from a person with monkeypox.

For more information, including guidance around sex visit [Monkeypox Facts for People Who are Sexually Active | Monkeypox | Poxvirus | CDC](#)







Isolation and infection control

[Infection control practices](#) for the care of people with monkeypox are the same regardless of HIV status. People with monkeypox [isolating at home](#) should also follow precautions to protect others in the household.

A person is contagious until after all the scabs on the skin have fallen off and a fresh layer of intact skin has formed underneath. Based on limited evidence from Ogoina et al, this period of contagiousness may be prolonged due to a longer period of illness in people with HIV who are not virologically suppressed.^[7] Decisions regarding discontinuation of [isolation precautions at a healthcare facility](#) and at home should be made in consultation with the local or state health department.

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