

Mpox



Mpox

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Clinical Considerations for Treatment and Prophylaxis of Mpox Infection in People Who are Immunocompromised

Updated April 3, 2023

Patients are still developing severe mpox. A [March 3, 2023, MMWR](#) provides updated clinical treatment considerations about using therapeutics to treat severe mpox cases, including ocular infections, neurologic complications, myopericarditis, complications associated with mucosal lesions, and complications from uncontrolled viral spread.

Summary of Changes

Updates as of December 13, 2022

- Expanded to include considerations for treatment and prophylaxis of mpox virus infection in people with immunocompromising conditions other than HIV.

Who this is for: Healthcare professionals caring for people who are immunocompromised from HIV or other conditions or who are taking immunosuppressive agents.

What this is for: Issues to consider when caring for people with or exposed to mpox who are also immunocompromised from a condition or from an immunosuppressive drug.

How to use: This information may be used to educate staff at healthcare facilities and by healthcare professionals developing mpox treatment and prophylaxis plans for people who have HIV or are immunocompromised or immunosuppressed from other conditions or treatments.

Key Points

- People with HIV-associated immunosuppression and people with HIV who are not virologically suppressed can be at increased risk of severe mpox.
- People who are immunocompromised from other conditions or using immunosuppressive agents may be at increased risk of severe mpox.
- Postexposure prophylaxis is available for people exposed to mpox virus and antiviral treatment(s) are available for people with mpox.
- Vaccination with JYNNEOS is considered safe for people who are immunocompromised, including those with HIV or primary immunodeficiency or from immunosuppressive therapies.
- Antiviral treatment(s) for mpox have minimal interaction with antiretroviral therapy and with common immunosuppressive medications.
- The use of tecovirimat for treatment of mpox should be considered in people who are immunocompromised. Addition of other therapeutics (cidofovir, brincidofovir, varicella immune globulin intravenous [VIGIV]) should be considered based on the clinical scenario.

- Screening for sexually transmissible infections (STIs), including HIV, should be considered for persons evaluated for mpox, with prompt care and treatment offered to those with positive test results.

These considerations are based upon limited evidence available to date about mpox in people who are immunocompromised. The approaches outlined below are intentionally cautious until additional evidence becomes available.

Immunosuppressive Conditions and Agents Considered for This Report

Moderate and severe immunocompromising conditions and treatments include but are not limited to:

- HIV infection, particularly in the presence of a low CD4 count (≤ 350 cells/mm³) or in the absence of viral suppression
- Moderate or severe primary immunodeficiency (e.g., phagocyte disorders, agammaglobulinemia, common variable immunodeficiency disease, severe combined immunodeficiency, DiGeorge syndrome, Wiskott-Aldrich syndrome, ataxia telangiectasia, or any other immunodeficiency with immune dysregulation)
- Active treatment for a solid tumor or hematologic malignancy
- Immunosuppressive therapy for solid-organ or islet transplant
- Active treatment with high-dose corticosteroids (i.e., 20 or more mg of prednisone or equivalent per day when administered for 2 or more weeks), an alkylating agent, antimetabolite, transplant-related immunosuppressive drug, cancer chemotherapeutic agent classified as severely immunosuppressive, tumor necrosis factor (TNF) blocker, or other biologic agent that is immunosuppressive or immunomodulatory
- Receipt of chimeric antigen receptor (CAR)-T-cell therapy or hematopoietic cell transplant (within 2 years of transplantation or taking immunosuppressive therapy)

Factors to consider when assessing the level of immune competence in a patient include underlying disease severity, duration, clinical stability, complications, comorbidities, and any potentially immune-suppressing treatment. For additional information about the degree of immune suppression associated with different medical conditions and treatments, providers can consult ACIP's [General Best Practices for Vaccination of People with Altered Immunocompetence](#), the [2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host](#) [↗](#), and the [AAP Red Book](#) [↗](#).

Mpox in People Who are Immunocompromised

There is a paucity of data regarding the severity of mpox in people who are immunocompromised, including those with uncontrolled HIV. However, people who are immunocompromised do appear to have higher risk of [vaccinia inoculation complications](#) following smallpox vaccination, larger and more widespread eruptions of [molluscum contagiosum](#), and recurrent or large [orf virus](#) lesions.¹ Additionally, a fatal case of cowpox virus infection has been previously reported in a recipient of a kidney transplant.² The generalizability of this evidence to mpox remains unknown.

Although they may have a higher risk of infection and severe illness, severe outcomes are not universally seen in people who are immunocompromised: one study from the 2003 outbreak of mpox in the United States noted recovery without severe disease in one patient with lupus nephritis and another patient with prior bone marrow transplant.³

Mpox in People With HIV

Available summary surveillance data from the European Union^{4,5,6}, England⁷, and the United States⁸ indicate that among gay, bisexual, and other men who have sex with men (MSM) with mpox for whom HIV status is known, 28%–51% have HIV infection. However, it is currently unknown whether an HIV infection increases a person's risk of developing mpox after exposure.

Mpox in People with HIV and Immunosuppression

- The available data indicate that people with advanced and uncontrolled HIV can be at a higher risk of severe or prolonged mpox. In a 2017–18 case series of 122 Nigerian patients with mpox, 4 of the 7 deaths occurred among people with untreated advanced HIV; however, data about the overall proportion of patients who had HIV were lacking.⁹
- A second 2017–18 case series, also reported 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, indicating immunosuppression. Compared with other patients, those with HIV had higher rates of secondary bacterial infections, more prolonged illnesses (and thereby also longer period of infectiousness), as well as a greater likelihood of a confluent or partially confluent rash, rather than discrete lesions.¹⁰
- In a [recent report from the U.S.](#), among persons with mpox, hospitalizations were more common in people with HIV than in those without HIV. CDC is aware of several cases of severe mpox among people with HIV who were immunocompromised; these patients required hospitalization, had prolonged disease courses, developed complications, and even had fatal outcomes.
- In limited published reports, mpox among people with advanced or untreated HIV has been associated with severe disease, including progressive or disseminated rash, protracted course, and complications including sepsis, ocular disease, encephalitis, and death.

Mpox in People with HIV Who Are Not Immunosuppressed

- In contrast, reports from European countries, where the majority of persons with HIV are taking antiretroviral therapy (ART) and have high CD4 cell counts, have not described excess hospitalizations among people who are coinfecting with HIV and mpox.^{2, 3, 4} The WHO has stated that “people with HIV...who take ART and have a robust immune system have not reported a more severe course of disease.” It is important to note that differences in disease severity may also be affected by the route of transmission, host susceptibility, and the quantity of mpox virus inoculated.¹¹

For additional information see [Severe Mpox in Hospitalized Patients—United States, August 10–October 10, 2022 | MMWR \(cdc.gov\)](#) and [Health Alert Network \(HAN\) 00475: Severe Manifestations of Mpox among People who are Immunocompromised Due to HIV or Other Conditions](#).

Incubation

It is not known whether the incubation of mpox differs between people who are immunocompromised and those who are immunocompetent. For details of the incubation period of mpox, see [Clinical Recognition](#).

Diagnosis

Clinical Picture

Fever and other prodromal symptoms such as chills, lymphadenopathy, malaise, myalgias, and headache may precede or follow the rash or be absent. It is not known whether the prodromal phase of mpox differs between people who are immunocompromised and those who are immunocompetent.

People who are immunocompromised 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.¹⁰ Rash presentations in people who are immunocompromised can also have coalescing or necrotic lesions. Additionally, people in this study with poorly controlled HIV were more likely to have prolonged illness.

See also [Severe Mpox in Hospitalized Patients — United States, August 10–October 10, 2022 | MMWR \(cdc.gov\)](#) and [HAN 00475: Severe Manifestations of Mpox among People who are Immunocompromised Due to HIV or Other Conditions](#).

Signs and Symptoms

In people who are immunocompromised, the [signs and symptoms](#) of mpox may be either similar (i.e., rash, fever, and lymphadenopathy) or dissimilar to those observed in people who are immunocompetent. In people who are immunocompromised, mpox may present with atypical manifestations or more severe illness (e.g., sepsis, disseminated rash, hemorrhagic disease, numerous confluent lesions, necrotic lesions, severe lymphadenopathy that can be obstructing, ocular or periorbital infections, pulmonary involvement, encephalitis, myocarditis or other conditions requiring hospitalization).¹²

For more information on severe disease caused by mpox see [Severe Mpox in Hospitalized Patients — United States, August 10–October 10, 2022 | MMWR \(cdc.gov\)](#) and [HAN 00475: Severe Manifestations of Mpox among People who are Immunocompromised Due to HIV or Other Conditions](#).

Differential Diagnosis

In people who are immunocompromised, [mpox](#) should be considered as a possible etiology of rash illness. Other etiologies to consider include herpes zoster (shingles), scabies, molluscum contagiosum, herpes simplex, enteroviral infection (hand-foot-and-mouth disease), syphilis, chancroid, lymphogranuloma venereum, and other infections which can cause cutaneous manifestations in immunocompromised hosts (e.g., endemic fungi, non-tuberculous mycobacteria), allergic skin rashes, and drug eruptions. Mpox can be confused with disseminated herpes zoster or herpes simplex virus infections. These herpes virus infections, and especially disseminated herpes zoster, most commonly affect people with immunocompromising conditions. Therefore, to establish a diagnosis for immunocompromised people who present with a rash, clinicians should elicit a medical history that includes a [detailed sexual health history](#) (i.e., partner number, frequency, activities), perform a complete physical examination, and order appropriate laboratory testing.




Coinfections

Mpox coinfections with STIs have been reported. [In a recent study](#), among 1,969 people with mpox in eight U.S. jurisdictions, 38% had HIV infection, and 41% had an STI in the preceding year. Therefore, people being evaluated for mpox should also be [tested, and treated as indicated, for HIV and other STIs](#).^{13, 14}

Laboratory Confirmation

For details on specimen collection and handling, please see: [Preparation and Collection of Specimens](#).

Treatment

Mpox in people who are immunocompetent tends to be a mild illness that resolves spontaneously. For such patients, supportive care, [pain management, skin care](#)  [\[165 KB, 2 pages\]](#) , and [wound care](#)  that is implemented early in the course of illness may be sufficient. However, prognosis depends on multiple factors, including initial health status, concurrent illnesses, previous vaccination history, and comorbidities.

People who are immunocompromised from HIV or other conditions or from immunosuppressive therapy may be at increased risk of severe prolonged mpox and protracted infectiousness. This appears to be most likely in those who are more severely immunocompromised. Although the available data are presently insufficient to define actionable thresholds, many severe outcomes have been observed in patients with CD4 counts $\leq 350/\text{mm}^3$ (who are unlikely to be virologically suppressed). Until more is known, clinicians should consider both viral suppression and CD4 count when evaluating the extent of immunosuppression (from HIV or any other sources) and assessing the risk for severe mpox. In patients deemed to be severely immunosuppressed based on clinical judgement, supportive care and pain control are unlikely to be sufficient.

Early [treatment targeting the virus itself](#) and visual [monitoring](#) should be considered for this population. Patients who have HIV who are not currently on ART, should be started or restarted on ART. The decision whether to treat and monitor a person who is immunocompromised in their home or in an inpatient setting should be individualized. If the patient fails to improve with a usual course (i.e., 14 days) of oral tecovirimat, consideration may be given to both extending the duration of therapy and changing the route of administration from oral to IV. Such considerations should be made on a case-by-case basis, taking into account the patient's condition, other comorbidities, ability to absorb oral medications, and ability to take a full, fatty


meal. Addition of other therapeutics, such as VIGIV, brincidofovir, or cidofovir may also be considered (see below). Decisions on whether and when to use medical countermeasures must be made individually for each person and can depend on a variety of clinical and other parameters.¹⁵

In such cases, consider consultation with infectious disease, public health experts, or CDC. The CDC clinical consultation service for patient management questions may be accessed by calling the CDC Emergency Operations Center (EOC) at (770) 488-7100.

Managing HIV in People with Mpox and HIV

ART and opportunistic infection prophylaxis should be continued in all people with HIV who develop mpox. ART interruption may lead to rebound viremia that could complicate the management of mpox (for example, worsen the severity of illness). People without HIV who are taking ART for HIV pre-exposure prophylaxis (PrEP) or postexposure prophylaxis (PEP) should also continue taking these medications.

People diagnosed with mpox who have HIV (even if newly diagnosed) who are not on ART should be started on ART as soon as possible in consultation with an expert in HIV medicine if needed. Consultation with CDC is encouraged for severe cases of mpox. The CDC clinical consultation service for patient management questions may be accessed by calling the CDC EOC at (770) 488-7100.

Clinicians using antivirals for mpox should be alert for drug-drug interactions with any antiretrovirals used to prevent^{16, 17} or treat¹⁸ HIV infection as well as with any other medications used to prevent or treat HIV-related opportunistic infections.¹⁹ Key critical interactions are discussed below for each mpox antiviral. Any potential drug-drug interactions not noted below can be assessed using the interactive [University of Liverpool HIV Drug Interactions database](#) .

Treatment of Mpox

Currently there is no treatment approved specifically for mpox. However, United States Government (USG)-stockpiled antivirals, developed for use in patients with smallpox, may be beneficial against mpox. The following medical countermeasures, currently available from the Strategic National Stockpile (SNS), are options for the treatment of mpox: tecovirimat, brincidofovir, and vaccinia immune globulin intravenous (VIGIV). Commercially available cidofovir is also an option.

Additional information on treatment can be found here: [CDC Treatment Information for Healthcare Professionals](#) and [FDA Mpox Response](#) .




Tecovirimat (also known as TPOXX)

[Tecovirimat](#) is an antiviral that inhibits the orthopoxvirus VP37 envelope wrapping protein. It is available as a capsule or an injection for intravenous (IV) administration and is approved by the United States Food and Drug Administration (FDA) for the treatment of smallpox in adults and children.




Although data are not available on the efficacy of tecovirimat for treating human mpox, studies using a variety of animal species have shown it to be effective for treating disease caused by orthopoxvirus.²⁰ A clinical trial focused on safety in healthy people without mpox showed the drug had an acceptable safety profile.²¹

Tecovirimat

- should be considered as first line treatment of mpox in people who have advanced or poorly controlled HIV or are otherwise immunocompromised, as they may be at high risk for severe disease. **It is important to begin tecovirimat as early as possible in such patients.**
- should be given IV if there is concern for inadequate or altered oral drug absorption or if the patient is unable to take oral therapy.
- consider extending tecovirimat beyond the standard 14-day course on a day-by-day basis.
- consider the addition of other therapies (e.g., cidofovir, brincidofovir, and VIGIV).

Providers can obtain tecovirimat for their patients in two ways: through an investigational new drug (IND) protocol or through a study. CDC holds an [expanded access IND protocol](#)  [475 KB, 24 pages] (sometimes called “compassionate use”) that allows stockpiled tecovirimat to be used to treat patients with mpox during an outbreak. Providers may also enroll their patients in the [AIDS Clinical Trials Group \(ACTG\) Study of Tecovirimat for Human Mpox Virus \(STOMP\) trial](#) , which is evaluating the efficacy of tecovirimat. In this study, all adults with severe mpox, severe immunodeficiency, or other [noted criteria](#)  will be enrolled in the open-label arm to receive oral tecovirimat. For additional information on how to obtain tecovirimat for a patient, please see: [Information for Healthcare Providers: Tecovirimat \(TPOXX\) for Treatment of Mpox](#).

Contraindications & Considerations for Use of Tecovirimat in People Who are Immunocompromised, Including from HIV

- Tecovirimat IV is contraindicated in patients with severe renal impairment e.g., creatinine clearance < 30 mL/min.
- Tecovirimat may increase the concentration of the blood glucose-lowering agent repaglinide and decrease the concentration of midazolam. Patients on repaglinide should be monitored for hypoglycemia.
- Tecovirimat might reduce somewhat the levels of the non-nucleoside reverse transcriptase inhibitor (NNRTI) rilpivirine. Therefore:
 - Long-acting cabotegravir/rilpivirine should not be started during tecovirimat therapy and for 2 weeks after the conclusion of tecovirimat.
 - For individual who have recently received their initial dose of long-acting rilpivirine/cabotegravir IM, consider adding oral rilpivirine 25 mg once daily during tecovirimat treatment and for 2 weeks after the end of treatment.
 - For patients already taking long-acting cabotegravir/rilpivirine or another rilpivirine-containing ART regimen and who require tecovirimat, experts believe no additional therapy is necessary during tecovirimat treatment. If there is a concern for suboptimal RPV exposure, seek expert consultation.
- Although the [tecovirimat eIND](#)  [475 KB, 24 pages] mentions drug interactions between tecovirimat and both doravirine and maraviroc, neither requires dose-adjustments when co-administered with tecovirimat.
- For additional resources to determine drug interactions and potential dosing modifications, please see: [University of Liverpool HIV Drug Interactions database](#)  and [Drug-Drug Interactions: ARVs and Treatments for Severe Mpox – AIDS Institute Clinical Guidelines \(hivguidelines.org\)](#) .
- Although few interactions are expected between standard immunosuppressive medications and tecovirimat,^[1] tecovirimat may reduce serum concentrations for tacrolimus and sirolimus. Close monitoring of tacrolimus and sirolimus levels are recommended, as dose increases may be required.

[1] Footnote: Medications specifically assessed: methotrexate, mycophenolate, azathioprine, cyclosporine, tacrolimus, sirolimus, everolimus, thymoglobulin, prednisone, methylprednisolone, dexamethasone, prednisolone, infliximab, adalimumab, etanercept, baricitinib, tofacitinib, upadacitinib, abatacept.

For additional information see [tecovirimat package insert](#)  [565 KB, 24 pages]  and [tecovirimat IND](#)  [475 KB, 24 pages].

Cidofovir (also known as Vistide)

Cidofovir has shown to be effective against orthopoxviruses in *in vitro* and *in vivo* studies. Although data are not available on the effectiveness of cidofovir for treating people with severe mpox and it is unknown whether someone with severe mpox will benefit, healthcare providers may consider the use of cidofovir in such patients. Cidofovir is commercially available.

Contraindications & Considerations for Use of Cidofovir in People Who are Immunocompromised, Including from HIV

- Dose-dependent nephrotoxicity is a concern with cidofovir, and it is contraindicated in patients with serum creatinine >1.5 mg/dL.
- Cidofovir should not be used simultaneously with brincidofovir.
- 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 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.

- No drug interactions are anticipated between cidofovir and standard immunosuppressive medications.
- Cidofovir has interactions, including contraindications for use, with other medications that should be assessed by the clinical team.

For additional information see [cidofovir package insert](#)  [830 KB, 6 pages] [↗](#).

Brincidofovir (also known as CMX001 or Tembexa)

[Brincidofovir](#) is a prodrug of cidofovir. It is available as oral tablets or suspension and is approved by the FDA for the treatment of smallpox in adults and children, including neonates.

Brincidofovir has been shown to be effective against orthopoxviruses in *in vitro* and *in vivo*. Although data are not available on the effectiveness of brincidofovir for treating people with severe mpox and it is unknown whether someone with severe mpox will benefit, healthcare providers may consider its use in such patients.

Brincidofovir is available through the SNS to clinicians who request and obtain an [FDA-authorized single-patient emergency use IND \(e-IND\)](#) [↗](#). To meet FDA's review criteria for a brincidofovir e-IND mpox treatment request, a patient with laboratory-confirmed (i.e., viral testing) mpox must have


- Current severe disease OR be at high risk for progression to severe disease AND
 - be ineligible for tecovirimat,
 - have a contraindication to oral or IV tecovirimat, OR
 - clinically deteriorate (i.e., significant disease progression or recrudescence [improvement followed by worsening]) while on tecovirimat.

Contraindications & Considerations for Use of Brincidofovir in People Who are Immunocompromised, Including from HIV

- Brincidofovir should not be used simultaneously with cidofovir. In contrast to cidofovir (which is associated with dose-dependent nephrotoxicity), serious renal toxicity or other adverse events have not been observed during treatment of cytomegalovirus infections with brincidofovir.
- Brincidofovir has clinically relevant drug interactions with protease inhibitors (PIs), cobicistat, and fostemsavir that may require modification of therapy. If PIs, cobicistat, or fostemsavir are co-administered with brincidofovir, clinicians should monitor closely for adverse reactions (for example, elevations in transaminase levels), and dosing of ART should be delayed for at least 3 hours after brincidofovir administration.
- Brincidofovir has interactions, including contraindications for use, with other medications that should be assessed by the clinical team.

For additional information see [brincidofovir package insert](#)  [465 KB, 21 pages].

Vaccinia Immune Globulin Intravenous (VIGIV)

[VIGIV](#) is an immune globulin intravenous that contains human vaccinia virus immunoglobulins that is used in the treatment of complications due to vaccinia vaccination. CDC holds an [e-IND protocol](#)  [400 KB, 25 pages] that allows the use of stockpiled VIGIV for the treatment of orthopoxviruses (including mpox) in an outbreak. Data are not available on the effectiveness of VIGIV in treatment of mpox. Although it is unknown whether someone with severe mpox will benefit from treatment with VIGIV, healthcare providers may consider its use in patients with severe mpox.

Contraindications & Considerations for Use of VIGIV in People Who are Immunocompromised, Including from HIV

- Glucose dehydrogenase pyrroloquinolinequinone (GDH-PQQ) or glucose-dye-oxidoreductase method (monitor and test strips) must not be used for blood glucose testing in patients receiving VIGIV, since maltose in IGIV products has been

shown to give falsely high blood glucose levels in these testing systems. Instead, blood glucose measurement in patients receiving VIGIV must be done with a glucose-specific method (monitor and test strips) to avoid interference by maltose contained in VIGIV.

- VIGIV is contraindicated in individuals with
 - a history of anaphylaxis or prior severe systemic reaction associated with the parenteral administration of this or other human immune globulin preparations.
 - Immunoglobulin A (IgA) deficiency with antibodies against IgA and a history of IgA hypersensitivity.

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

- Mpox 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. This finding, however, has not been noted in other studies. Therapeutic considerations for ocular mpox are included in the [guidance on management of ocular mpox](#).
- There are no specific contraindications for use of VIGIV among people who are immunocompromised, including with HIV. There are no known or anticipated interactions with ART or immunosuppressive medications.

For additional information see [VIGIV package insert](#)  and [VIGIV e-IND](#)  [400 KB, 25 pages].

Vaccination

Mpox Pre- and Postexposure Prophylaxis

Pre-Exposure Prophylaxis

The risks and benefits of pre-exposure prophylaxis (PrEP) by vaccination should be discussed with [people who are immunocompromised](#). There are two vaccines, JYNNEOS® and ACAM2000®.

- Only JYNNEOS should be used when pre-exposure prophylaxis by vaccination is chosen in someone who is immunocompromised or in someone who has HIV, whether they are immunocompromised or not.
- ACAM2000 should not be used in anyone who is immunocompromised, as it poses a risk of serious complications from enhanced replication of vaccinia virus.

Postexposure Prophylaxis

Postexposure prophylaxis (PEP) [vaccination for mpox](#) should be offered to people who are immunocompromised, including from HIV [as indicated](#). The benefits and potential adverse effects of PEP vaccination should be discussed with the person using shared decision-making. Although the efficacy of these therapies for mpox PEP is unknown,

- early use of vaccination (within 4 days from exposure) could prevent mpox, later use (5 days or more after exposure) may decrease the severity of mpox if infection does occur.
- in a person who is severely immunocompromised with a known high-risk exposure (who is at risk for severe mpox), the benefits of vaccination more than 14 days after exposure [may still outweigh risks](#).

Similar to PrEP, the risks and benefits of PEP by vaccination should be discussed with [people who are immunocompromised](#).

- Only JYNNEOS should be used when PEP vaccination is chosen in someone who is immunocompromised.
- ACAM2000 should not be used in anyone who is immunocompromised, as it poses a risk of serious complications from enhanced replication of vaccinia virus.

Other therapies, including the antiviral medication tecovirimat and VIGIV, may be considered for mpox PEP on a case-by-case basis in an exposed person with severe immunodeficiency in T-cell function. Factors to consider include known [high-risk exposure](#) to a confirmed or probable case of infection and clinical conditions that necessitate an alternative option to PEP vaccination.

For more information on vaccination, please see [Mpox Vaccine Information for Healthcare Professionals](#) and [Interim Clinical Considerations for Use of JYNNEOS and ACAM2000 Vaccines during the 2022 U.S. Mpox Outbreak](#).

Timing of Vaccination

Timing of vaccination should take into consideration current or planned immunosuppressive therapies, optimization of both the person's medical condition and anticipated response to vaccination, and individual benefits and risks.

Vaccines for PEP should not be delayed in [patients taking immunosuppressive therapies](#). Ideally, orthopoxvirus vaccines should be administered at least 2 weeks before initiation or resumption of immunosuppressive therapies. For patients who receive B-cell-depleting therapies on a continuing basis, vaccines should be administered approximately 4 weeks before the next scheduled therapy.

The [utility of serologic testing](#), cellular immune testing, or B-cell quantification to assess immune response to vaccination and guide clinical care has not been established. Such testing outside of the context of research studies is not recommended at this time.

Vaccine Safety and Efficacy

Modified Vaccinia Ankara (also known as JYNNEOS)

[Modified vaccinia Ankara \(MVA\)](#) is a two-dose nonreplicating live virus vaccine.²² It is licensed by FDA for prevention of both smallpox and mpox disease in adults 18 years of age and older. Because MVA is replication-deficient, it poses no risk for

- progressive vaccinia
- autoinoculation (i.e., transfer of vaccinia virus from one part of the body to another)
- inoculation of others who come into contact with the vaccination site.

Therefore, MVA can be administered to people who are in contact with household members who are immunocompromised.

Available human data on MVA administered to people who are immunocompromised are insufficient to determine efficacy. MVA is considered safe for people with immunocompromising conditions; however, people who are immunocompromised may be less likely to mount an effective immune response after vaccination. There are limited data available regarding safety and efficacy of MVA in people who are immunocompromised except for studies regarding people with HIV. Specifically, one study enrolled people with a prior diagnosis of AIDS who were virologically suppressed and had CD4 counts between 100 and 500 and found no serious safety concerns; two doses produced neutralizing antibodies in 100% of people who were immunocompromised.^{23, 24}

Studies regarding safety and efficacy of MVA in people who are immunocompromised are also limited. MVA was studied in an immunocompromised macaque animal model as a potential vaccine vector without any substantial safety concerns.²⁵ Another study evaluated the safety and immunogenicity of MVA in a small number of people with prior hematopoietic stem cell transplant and found that MVA was safe and immunogenic in this population.²⁶

Although an intradermal route of [administration](#) has been shown to be immunologically noninferior to a subcutaneous route in people who are immunocompetent, no data are available comparing safety and immunogenicity of these two routes in people who are immunocompromised. However, the risk for serious adverse events with either route is expected to be low. Intradermal administration of MVA is [currently recommended](#) for people who are immunocompromised.

For additional information see [MVA package insert](#) and the [MVA Emergency Use Authorization](#).

ACAM2000

[ACAM2000](#) is a single-dose live virus vaccine that uses replication competent 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
- congenital or acquired immune deficiency disorders due to a higher risk of adverse events.

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 conditions
 - have an immunocompromising condition
 - are pregnant
 - are aged <1 year

Household contacts include people with prolonged intimate contact with the potential vaccinee (for example, sexual contacts) and others who might have direct contact with the vaccination site or with potentially contaminated materials (for example, clothing or vaccination site dressings).

For additional information see [ACAM2000 package insert](#) and the [ACAM2000 IND](#).






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 mpox 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 EOC Watch Desk at (770)-488-7100.

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