

Mpox

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Epidemiology

Mpox (formerly monkeypox) is a zoonotic viral disease caused by monkeypox virus (MPXV), an enveloped double-stranded DNA virus that belongs to the *Orthopoxvirus* genus of the Poxviridae family, which also includes the causative agent of smallpox. MPXV circulates among certain small mammals found in the forested regions of western and central Africa, creating a reservoir of disease in the animal population that is believed to have been the source of the first human case in 1970.¹ Infections remained limited to western and central Africa, with rare travel-related cases outside this region until 2022. Two main clades of MPXV have been described in different geographic regions of Africa; clade I (previously called Congo Basin clade) has historically been associated with more severe disease and more human-to-human transmission than clade II (previously called West African clade).²⁻⁴ Each clade has two distinct subclades: clades Ia and Ib, and clades IIa and IIb.⁵

During May 2022, a multinational outbreak of clade II (subclade IIb) mpox emerged, causing more than 100,000 illnesses in over 120 countries as of November 2024.⁶ This outbreak was largely controlled by 2023; however, in the United States, clade IIb MPXV continues to circulate at low levels.⁶ The majority of infections have been transmitted sexually through intimate contact with one or more mpox lesions on the skin or mucosal surfaces of people with mpox.⁷ Transmission has also rarely occurred through occupational exposure through injuries via contaminated sharps. In the United States, infections have disproportionately affected gay, bisexual, and other men who have sex with men (MSM). Infections in women and children have been reported.⁸⁻¹⁶ Among MSM, coinfection with HIV and other sexually transmitted infections (STIs) has been common.⁸ Across reports, around 40 to 50% of cases have been in people with HIV, and around 15 to 30% of cases have been diagnosed concomitantly with gonorrhea, syphilis, chlamydia, or other STIs.^{8,9,17,18} Severe and fatal cases have disproportionately been reported in people with HIV, especially among people with advanced or uncontrolled HIV.¹⁹⁻³⁰ Although the overall mortality rate for clade II infection is low (<1%), mortality risk is higher among people with HIV that is advanced or not virologically suppressed.²⁶⁻³³

During January 2024, a separate outbreak of clade I mpox emerged in the Democratic Republic of Congo and spread to parts of eastern and southern Africa. Cases of clade I mpox outside of Africa have been rare and, as of this writing, are limited to individual travelers returning from Africa and their immediate household contacts.^{6,34,35}

Clinical Manifestations

In outbreaks prior to 2022, mpox cases had been characterized by prodromal symptoms of fever, headache, lymphadenopathy, myalgias, or fatigue followed by a [distinctive rash](#) that progressed synchronously from macules to papules, vesicles, pustules, and, ultimately, crusted lesions. People with advanced HIV experienced longer duration of illness, larger sized lesions, more frequent secondary bacterial infections, and the presence of genital ulcers.^{29,31}

During the 2022 multinational mpox outbreak and among ongoing cases in the United States, the clinical manifestations associated with clade II infection are distinct in several respects.^{9,36} Prodromal symptoms have been mild or absent and have not always preceded the rash.³⁶ Rash commonly occurs as anogenital or oropharyngeal/perioral lesions but has also involved the limbs, face, and trunk.^{9,36} Lesions can be single or multiple, limited to a single body site, and can progress in varying stages asynchronously.^{9,36} Inguinal, cervical, and/or axillary lymphadenopathy can be present but not as reliably as with classic presentations.³⁶

People with well-controlled HIV typically experience self-limiting disease and recover with supportive care alone.³⁷ Nonetheless, mpox can cause significant pain, especially in sensitive anatomic sites, including the oropharynx, genitals, and anorectum, where it can lead to other complications. Pharyngeal involvement can result in tonsillitis or pharyngitis associated with odynophagia or dysphagia.⁹ Inflammation from genital lesions can produce dysuria, occasionally complicated by significant paraphimosis/phimosis or urethritis that limits the ability to urinate.^{30,38,39} Anorectal involvement can cause tenesmus, proctitis, and rectal bleeding.^{9,40} Gastrointestinal manifestations, such as enteritis or colitis, and anogenital involvement can necessitate hospitalization for enhanced symptom control or pain management.^{9,30,39} Lesions have led to stricture and scar formation, causing urethral or bowel obstruction.^{30,39} Ocular involvement from autoinoculation can result in conjunctivitis, blepharitis, keratitis, corneal ulcer with possible scarring, and, in rare cases, loss of vision.⁴¹⁻⁴³ Bacterial superinfections (e.g., staphylococcal skin and soft tissue infections) can also occur.³⁰ Other reported manifestations have included necrotizing digestive tract lesions, diffuse nodular pulmonary disease with infarcts and bronchopneumonia, encephalitis and transverse myelitis, myocarditis and pericarditis, septic arthritis, viral cold abscesses, and genital necrosis.^{30,44-46}

People with HIV and significant immunocompromise (i.e., unsuppressed viral load or CD4 T lymphocyte [CD4] cell count <200 cells/mm³ and especially <50 cells/mm³) are more likely to experience prolonged and progressive illness leading to hospitalization or death.^{19-30,37,47,48} Illness can include coalescing or necrotic lesions of the skin and mucosa that require surgical debridement. These lesions can continue to enlarge and deepen, despite initiation of medical treatment for mpox (see [Treating Disease](#) below).⁴⁹⁻⁵¹

Cases among pregnant women have been less common and not yet been associated with severe disease.^{52,53}

Although the clinical presentation of clade I infection overlaps closely with that of clade II (i.e., fever, lymphadenopathy, malaise, and a centrifugal rash with classic lesions), overall, the severity of these signs and symptoms are typically greater with clade I illness.^{2,54-58} Historically, illness from clade I infection has exhibited a greater case fatality rate than clade II in Africa; however, access to robust supportive care is expected to substantially decrease clade I fatalities.^{2,54-58}

Diagnosis

A high index of suspicion is warranted for mpox. Clinical presentation with symptoms such as a characteristic rash is strongly suggestive of mpox.⁵⁹ However, diagnosis of mpox based solely on clinical presentation can be challenging. Illness can be atypical, with isolated proctitis or rectal bleeding, or a small number of lesions. Skin and mucosal lesions can mimic lesions seen in other infections, such as herpes zoster, herpes simplex, syphilis, and molluscum contagiosum. For these reasons, and due to the high frequency of coinfection with STIs seen during the multinational 2022 clade II mpox outbreak, a broad differential diagnosis is encouraged for all people undergoing

evaluation for mpox. Screening for STIs, including HIV, is recommended where sexual exposure to mpox might have occurred.⁸

Mpox can be confirmed by the presence of viral DNA in a clinical specimen using polymerase chain reaction (PCR).^{7,59} The recommended specimen is skin lesion material, which can include swabs of a lesion's surface, lesion exudate, or lesion crusts. In the absence of a lesion on epithelialized skin, specimens from mucosal (e.g., oropharynx, anorectum) lesions or tissues can support diagnosis of mpox.^{9,60-62} Unroofing or aspirating lesions is neither required nor recommended and has led to occupational infections from injuries with contaminated sharps; vigorous swabbing of lesion surfaces alone is sufficient.^{13,14,63} Testing is available through state public health laboratories and multiple commercial laboratories. Check with your local institution or public health department for instructions on specimen collection and transport.

Mpox diagnosis can also be established by serologic testing that demonstrates detectable levels of anti-*Orthopoxvirus* immune globulin M antibody within 4 to 56 days after rash onset in the absence of recent mpox vaccination.⁵⁹ If there is high clinical suspicion for mpox and inconclusive or negative testing via PCR or antibody testing, additional testing can be used to confirm diagnosis. Options include next-generation sequencing, viral culture to demonstrate the presence of replication-competent virus, biopsy with immunohistochemical staining to demonstrate the presence of viral antigen, or electron microscopy to demonstrate the presence of characteristic viral particles; however, these diagnostic technologies have varying availability.⁵⁹

Clade I infection outside of Africa remains rare and limited mostly to travelers. Thus, the Centers of Disease Control and Prevention (CDC) recommends that patients with suspected mpox undergo clade-specific testing if they have traveled to affected areas of central and eastern Africa within 21 days of illness onset.⁶⁴ See CDC's [Clade I Mpox Outbreak Originating in Central Africa](#) webpage for a list of such countries affected by mpox. Clinicians pursuing clade-specific testing should consult with their state health departments for details about specimen collection and transport.^{65,66}

Preventing Exposure

Strategies to prevent mpox exposure are similar for people with and without HIV.⁶⁷ Regardless of vaccination status, people with HIV should avoid direct contact (including sex) with people who may have symptoms of mpox, avoid surfaces or objects that may have been used by someone with mpox, and frequently wash hands after contact with rash material or contaminated surfaces (**AIII**). Condoms or other barrier methods might provide additional protection during sex or other intimate activity. During active mpox outbreaks when rates of community transmission are elevated, it is recommended that all people (including people with HIV) be counseled about the value of temporarily reducing their number of sexual partners and limiting visits to venues where group sex or other prolonged skin-to-skin contact is possible (**CIII**).

For clinicians managing patients with confirmed or suspected mpox, the recommended personal protective equipment includes gowns, gloves, eye protection, and N95 masks. Procedures that could cause the spread of oral secretions should be performed in an airborne infection isolation room. Self-inoculation with sharps contaminated with monkeypox virus has been the leading cause of health care-associated infections.^{13-16,68,69} Thus, as noted above (see Diagnosis section), it is neither necessary nor recommended that lesions be unroofed using sharps when collecting diagnostic samples. See CDC's [Mpox Infection Prevention and Control in Healthcare Settings](#) webpage for additional infection control recommendations.

Preventing Disease

Vaccination is the principal biomedical means of preventing mpox, regardless of clade. Mpox vaccination should be offered to all people with HIV who have not had prior mpox and who have or anticipate potential exposure to mpox, regardless of CD4 count, per CDC's [interim clinical considerations](#) **(BII)**.⁷⁰

For unvaccinated people with HIV who experience a known or presumed exposure, post-exposure vaccination is recommended as soon as possible, per CDC's [interim clinical considerations](#).⁷¹

On a case-by-case basis and in consultation with an infectious disease expert and the CDC, drugs used to treat mpox (i.e., tecovirimat, vaccinia immune globulin intravenous [VIGIV]) can be considered for mpox post-exposure prophylaxis for people with HIV who have advanced immunosuppression or a contraindication to vaccination. Currently, clinical data are incomplete regarding the effectiveness of mpox post-exposure prophylaxis with these agents.

For additional details on mpox immunizations for pre- and post-exposure prophylaxis, see the [Mpox vaccine section](#) of the Immunization chapter.

Treating Disease

Recommendations for Treating Mpox
<p>General Considerations</p> <ul style="list-style-type: none">• Mpox is typically a self-limiting illness that resolves spontaneously in people with well-controlled HIV. People with mild to moderate mpox who are not at high risk for severe disease should be managed with supportive care, including adequate pain control (BIII), and be offered referral to clinical trials of mpox treatment, if available (CIII).• People with HIV who have severe mpox* or are at high risk for severe mpox** should receive directed mpox antiviral treatment (BIII). The Panel recommends early consultation with the CDC or an expert in mpox treatment and prompt use of combination therapy, ideally at the time of the first medical encounter and after considering the risks and benefits (CIII). Providers can reach CDC's clinical consultation service via email (poxvirus@cdc.gov) or by calling the CDC Emergency Operations Center at 770-488-7100.• People with severe immunocompromise might benefit from extended treatment (i.e., >14 days) if new confirmed mpox lesions occur or existing lesions or symptoms worsen despite treatment (CIII).• People with HIV not taking effective ART at the time of mpox diagnosis should initiate an effective antiretroviral regimen as soon as possible (AIII). <p>Preferred Therapy for Severe Disease* or People at Risk for Severe Disease**</p> <ul style="list-style-type: none">• Tecovirimat is available via an EA-IND protocol and can be considered for patients who meet the EA-IND criteria. For patients who do not meet inclusion criteria, supportive care is recommended (AII). See text for details.• Tecovirimat 600 mg PO every 12 hours (for weight 40 kg to <120 kg) or every 8 hours (for weight ≥120 kg) for 14 days; each dose should be taken within 30 minutes of a high-fat meal (BIII); <i>or</i>• Tecovirimat 200 mg IV every 12 hours for 14 days (for weight 35 kg to <120 kg) or 300 mg IV every 12 hours (for weight ≥120 kg) infused over 6 hours (BIII)• IV therapy is indicated if concern exists regarding altered gastrointestinal absorption, inability to take PO medications, or severity of illness. <p>Adjunctive Therapy for Severe Disease or People at Risk for Severe Disease*</p>

Prompt use of combination therapy, in consultation with the CDC or an expert in mpox treatment and after considering risks and benefits, is recommended (CIII). Cidofovir or brincidofovir can be used as adjunctive therapy in people with or at risk for severe disease or in people who experience clinically significant progression while receiving tecovirimat, develop recrudescence of disease after an initial period of improvement while receiving tecovirimat, or are otherwise ineligible to receive oral or IV tecovirimat (BIII). VIGIV can be used in severe cases where the development of a robust antibody response may be impaired (BII).

- Cidofovir 5 mg/kg IV once weekly for 2 weeks. Each dose should be given with saline hydration before and after therapy plus probenecid 2 g PO 3 hours before the dose followed by 1 g PO 2 hours after the dose and 1 g PO 8 hours after the dose (total of 4 g) (BIII).

or

- Brincidofovir 200 mg PO once weekly for two doses (BIII)
 - Brincidofovir is available via a single-patient [emergency use IND authorization for treatment of mpox](#).
 - Male patients should be counseled on the risk for irreversible effects of brincidofovir on male fertility (AII).
 - Women of childbearing potential should use effective contraception and/or condoms during treatment and for at least 4 months after the last dose (AIII).

or

- VIGIV 6,000–9,000 units/kg IV single dose (BIII)
 - VIGIV is available via an [expanded access IND](#).
 - Repeat doses may be considered on a case-by-case basis in consultation with the CDC (BIII).
 - Vaccination with any live virus vaccines should be delayed until 3 months after VIGIV administration (CIII). People who received VIGIV shortly after a live virus vaccination should be revaccinated 3 months after administration of the immune globulin (CIII).

Preferred Therapy for Ocular Mpox

- Tecovirimat 600 mg PO every 12 hours (for weight 40 to <120 kg) or every 8 hours (for weight ≥120 kg) for 14 days within 30 minutes of a fatty meal (BIII), *plus*
- Trifluridine (Viroptic) 1 drop into affected eye(s) every 2 hours when awake (max: 9 drops/day) until reepithelialization, then every 4 hours (min: 5 drops/day) for 7 days, or until all periocular lesions have healed (BIII)
 - Trifluridine should be used in consultation with an ophthalmologist (BIII).
 - Prolonged use of trifluridine beyond 21 days might cause corneal epithelial toxicity and should be avoided (AII).

Pregnancy Considerations

- Pregnant, recently pregnant, or breastfeeding women should be offered treatment for mpox (AIII).
- Tecovirimat is available through CDC-sponsored EA-IND for women who are pregnant or breastfeeding (BIII).
- In animal studies, cidofovir and brincidofovir have been shown to be teratogenic; therefore, these agents are not recommended for use during pregnancy (AIII).

* Severe mpox might manifest as hemorrhagic disease; lesions affecting 25% or more of body surface that may be confluent, necrotic, and/or hemorrhagic in appearance or cause sepsis; disease resulting in airway compromise or affecting the nervous system; cardiac and/or neurologic disease; ocular or periorbital infections; or other conditions requiring hospitalization.

** People with HIV at risk for severe mpox include people who are not virologically suppressed, have CD4 counts <200 cells/mm³, have another immunocompromising condition, have atopic dermatitis or other conditions affecting skin integrity, or are children, pregnant, or breastfeeding. Consult CDC's [Tecovirimat webpage](#) for more details.

Key: ART = antiretroviral therapy; CD4 = CD4 T lymphocyte; CDC = Centers for Disease Control and Prevention; EA-IND = expanded access investigational new drug; IND = investigational new drug; IV = intravenous; the Panel = Panel on

Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV; PO = orally; VIGIV = vaccinia immune globulin intravenous

Mpox is typically a self-limiting illness that resolves spontaneously in people with well-controlled HIV. People with mild to moderate mpox and who are not at high risk for severe disease should be managed with supportive care, including adequate pain control (**BIII**), and be offered referral to clinical trials of mpox treatment, if available (**CIII**). The CDC offers a clinical consultation service (email poxvirus@cdc.gov), or health care providers may contact the CDC Emergency Operations Center at 770-488-7100, where the CDC can provide additional guidance to clinicians with patient management questions.

People with HIV experiencing or at high risk of developing more severe, prolonged, and potentially life-threatening mpox (e.g., have CD4 counts <200 cells/mm³ or are otherwise severely immunocompromised) should receive directed mpox antiviral treatment (**BIII**).³⁷ The Panel recommends early consultation with the CDC or an expert in mpox treatment and the prompt use of combination therapy, ideally at the time of the first medical encounter and after considering the risks and benefits (**CIII**). People with severe immunocompromise might benefit from extended treatment (i.e., >14 days) if new confirmed mpox lesions occur or existing lesions or symptoms worsen despite treatment (**CIII**).

Clinicians can request and obtain tecovirimat for non-research single-patient use through a CDC-sponsored [expanded access investigational new drug \(EA-IND\) protocol](#), and it might also be available through clinical trials. At this time, tecovirimat under the EA-IND is available for people with HIV who have a CD4 count <200 cells/mm³ or are experiencing certain immunocompromising illnesses or undergoing certain immunocompromising treatments, are experiencing atopic dermatitis or other conditions affecting skin integrity, are children, are pregnant, or are breastfeeding. For patients who do not meet inclusion criteria, supportive care is recommended (**AII**).

Tecovirimat, which inhibits the *Orthopoxvirus* VP37 envelope-wrapping protein, is available as an oral capsule or intravenous (IV) injection. Clinical trials have demonstrated the drug has an acceptable safety profile,⁷²⁻⁷⁴ and observational data have suggested that tecovirimat might hasten subjective symptomatic improvement in patients with severe mpox.⁷⁵ However, two randomized, placebo-controlled double-blind trials found tecovirimat provided no efficacy against mpox. Specifically, the PALM007 trial conducted in the Democratic Republic of Congo⁷⁶ demonstrated no difference in the time to mpox lesion resolution⁷⁷ in people with clade I infection, and the international STOMP trial⁷⁸ was stopped early for futility because it neither improved time to lesion resolution nor improved self-reported pain scores or pain duration in patients with mild to moderate illness from clade II infection.⁷⁷ As a result, in the United States, non-research access to tecovirimat for people with HIV is currently limited to patients who have a CD4 count <200 cells/mm³ or are severely immunocompromised, have atopic dermatitis or other conditions affecting skin integrity, are children, are pregnant, or are breastfeeding (**BIII**).

The decision to use oral or IV tecovirimat should be based on the severity of illness (e.g., extent of other organ systems affected by mpox, presence of coalescing nonhealing lesions), other comorbidities that could contribute to greater severity of illness, expected adherence to the oral formulation, and gastrointestinal absorption capacity.³⁷ Oral tecovirimat requires intact gastrointestinal absorption and the ability to consume a high-fat meal (600 calories and 25 g fat) when dosed to support absorption.⁷⁹

IV cidofovir or oral brincidofovir can be used as adjunctive therapy in people with or at risk for severe disease or in people who experience clinically significant progression while receiving tecovirimat, develop recrudescence of disease after an initial period of improvement while receiving tecovirimat, or are otherwise ineligible to receive oral or IV tecovirimat (**BIII**). Cidofovir, which acts via competitive inhibition of DNA polymerase to block DNA synthesis of many DNA viruses, is an U.S. Food and Drug Administration–approved antiviral medication for the treatment of cytomegalovirus retinitis in people with advanced HIV. Brincidofovir is a prodrug of cidofovir that acts similarly and is associated with less nephrotoxicity. There are insufficient clinical trial data on the effectiveness of cidofovir or brincidofovir in treating human mpox, including in people with HIV. However, *in vitro* and animal studies have demonstrated that these drugs are effective against other *Orthopoxviruses*.⁸⁰⁻⁸⁵ Data from animal models suggest that the combination of tecovirimat and brincidofovir might act synergistically to improve outcomes and could be considered for patients with disseminated infection (**CIII**).⁸⁶ A randomized, placebo-controlled trial to assess safety and efficacy of brincidofovir for mpox treatment is ongoing in Africa.⁸⁷ Presently, brincidofovir is only available from federal partners to clinicians who request and obtain a single-patient [emergency use IND authorization for treatment of mpox](#). Clinicians should consider the side effect profiles of both medications when deciding on their use (see [Table 5. Serious and/or Common Adverse Reactions Associated With Systemically Administered Drugs Used to Treat or Prevent Opportunistic Infections](#) for more information).

VIGIV can be used in severe cases where the development of a robust antibody response may be impaired (**BIII**). Data are not available on the effectiveness of VIGIV to treat human mpox, including in people with HIV. In animal models using non-human primates, vaccine-induced vaccinia antibodies were protective against the lethal challenges of monkeypox virus. The benefit of VIGIV for treatment of severe mpox is unknown. VIGIV is administered under a [specific CDC protocol](#). Subsequent dosing (i.e., redosing) decisions should be made on a case-by-case basis in consultation with the CDC and can be considered when mpox lesions affect a large percentage of a person’s body surface at the time of diagnosis (e.g., 25%), new lesions emerge or borders on existing lesions enlarge several days after administration of VIGIV, lesions affect mobility or are concerning for long-term sequelae (such as sexual dysfunction), or adverse events or contraindications preclude maximal use of other medical countermeasures (**BIII**).³⁷

For people for whom VIGIV might be considered as pre-exposure prophylaxis, VIGIV might theoretically impair the efficacy of live attenuated replicating virus vaccines; however, the extent to which VIGIV might affect live attenuated nonreplicating vaccines, such as JYNNEOS, is unclear.⁸⁸ Thus, vaccination with any live virus vaccines should be delayed until 3 months after VIGIV administration (**CIII**).⁸⁸ People who receive VIGIV shortly after a live virus vaccination should be revaccinated 3 months after administration of the immune globulin (**CIII**).⁸⁸

The role of topical therapy in the treatment of mpox remains unknown. Topical cidofovir has been used for skin lesions with mixed success.^{89,90} For ocular involvement, trifluridine, in addition to systemic therapy, can be used in cases of MPXV conjunctivitis and is recommended in cases of MPXV keratitis, in consultation with an ophthalmologist (**BIII**).^{41,91,92} Prolonged use of trifluridine beyond 21 days might cause corneal epithelial toxicity and should be avoided (**AII**).⁹³

Treatments for mpox have the potential for complex and possibly bidirectional interactions with certain antiretroviral agents. See [Drug–Drug Interactions](#) in the Adult and Adolescent Antiretroviral Guidelines for recommendations regarding therapeutic drug monitoring and dosage adjustments, where feasible.

Vaccines and therapeutics active against clade II mpox are expected to be equally active against clade I.

Special Considerations With Regard to Starting Antiretroviral Therapy

People with HIV not presently taking effective antiretroviral therapy (ART) when diagnosed with mpox should initiate an effective antiretroviral regimen as soon as possible to improve T and B cell function, which have key roles in modulating mpox disease severity and preventing mortality **(AIII)**.^{37,94-96}

Monitoring of Response to Therapy and Adverse Events (Including Immune Reconstitution Inflammatory Syndrome)

As with other opportunistic infections in people with advanced HIV, concerns have been raised about possible dysregulated immune responses, such as immune reconstitution inflammatory syndrome (IRIS), following initiation of ART.²⁶ IRIS could lead to paradoxical worsening or a protracted course of mpox disease. Data are insufficient to inform recommendations on the identification and management of dysregulated immune responses in the setting of mpox infection in people with advanced HIV. Providing passive immunity with the use of VIGIV and extending the duration of antivirals such as tecovirimat should be considered pending immune recovery **(CIII)**. VIGIV has an estimated half-life of up to 3 weeks. If immune reconstitution is slow, repeat VIGIV dosing should be considered on a case-by-case basis, as noted above **(BIII)**.

Monitoring is recommended during and after treatment of mpox to detect drug toxicity, as well as persistence or recurrence of mpox. The most common adverse effects of tecovirimat are headache and nausea.⁷⁹ For patients with severe renal impairment (creatinine clearance [CrCl] <30 mL/min), the IV formulation of tecovirimat should not be used due to the accumulation of an excipient (hydroxypropyl-beta-cyclodextrin) that has shown potential for nephrotoxicity at very high exposure levels **(BIII)**. Exceptions may be considered in consultation with the CDC. Renal function should be closely monitored if the IV formulation is used; if renal toxicity is suspected, consult with the CDC on switching to oral tecovirimat (if possible) or using an alternative agent **(BIII)**. See [Table 6. Dosing Recommendations for Drugs Used to Treat or Prevent Opportunistic Infections that Require Dosage Adjustment in Adults With Renal Insufficiency](#) for renal dosing information.

Adverse effects of cidofovir include dose-related nephrotoxicity, neutropenia, uveitis, and hypotony (low intraocular pressure).⁹⁷ The risk of severe renal injury from IV cidofovir can be reduced by prehydration and oral probenecid before and after cidofovir administration. In people receiving IV cidofovir, analysis of blood urea nitrogen and creatinine levels and urinalysis should be performed before each infusion.⁹⁷ Cidofovir administration is **contraindicated** if renal dysfunction or substantial proteinuria is detected (a serum creatinine >1.5 mg/dL, CrCl ≤55 mL/min, or a urine protein ≥100 mg/dL [equivalent to ≥2+ proteinuria]).⁹⁷ Particular attention is needed for patients receiving other potentially nephrotoxic medications, including tenofovir disoproxil fumarate.⁹⁷ Periodic (e.g., weekly) ophthalmologic examinations are recommended to monitor for cidofovir-associated uveitis or hypotony.⁹⁷

Adverse effects of brincidofovir include diarrhea, nausea, and other gastrointestinal adverse events, such as elevations in both hepatic enzymes (e.g., alanine transaminase, aspartate aminotransferase) and bilirubin.⁹⁸ Brincidofovir-induced diarrhea may impair absorption of oral tecovirimat. Screening for liver test abnormalities should be performed before starting therapy with repeat testing during

follow-up as clinically indicated.⁹⁸ Since brincidofovir is usually given only in two doses 1 week apart, monitoring of liver function parameters is generally done before the second dose (Day 8).⁹⁸ If serum aminotransferases are elevated and persist above 10 times the upper limit of normal, consider not giving the second dose of brincidofovir.⁹⁸ Do not give the second dose of brincidofovir on Day 8 if elevation of serum aminotransferases is accompanied by clinical signs and symptoms of liver inflammation or increasing direct bilirubin, alkaline phosphatase, or international normalized ratio.⁹⁸ Male patients should be counseled on the risk for irreversible effects on male fertility based on testicular toxicity observed in animal studies (**AII**).⁹⁸ Women of childbearing potential should use effective contraception and/or condoms during treatment and for at least 4 months after the last dose due to the teratogenic effect of brincidofovir (**AIII**).⁹⁸

Managing Treatment Failure

Clinical failure of therapy for mpox is more likely in patients who do not have substantial immune reconstitution after initiation or optimization of ART or who are otherwise severely immunocompromised. Treatment failure can also result from inadequate therapeutic drug levels secondary to inadequate gastrointestinal absorption, nonadherence, or drug resistance.

Tecovirimat has a relatively low barrier to viral resistance. Single amino acid substitutions at various locations in the F13L gene coding the viral VP37 drug target confer substantial reductions in tecovirimat's antiviral activity.⁷⁹ Genotypic and phenotypic resistance to tecovirimat has been documented in patients with severe immunocompromising conditions who have disseminated and progressive mpox infection and have received or are undergoing prolonged tecovirimat treatment.⁹⁹ Community transmission of a tecovirimat resistance-associated mutation has also been reported.¹⁰⁰

For people with documented or suspected tecovirimat resistance (e.g., new lesions form after the first 7 days of the 14-day regimen), additional therapeutics can be considered, including cidofovir or brincidofovir and VIGIV. Efforts should be made to ensure adherence and gastrointestinal absorption, and to maximize immune function by ensuring receipt of effective ART and limiting the use of immunocompromising therapies.³⁷

If new lesions occur or existing lesions worsen or other clinical manifestations do not improve during the initial 14-days of antivirals, extending treatment might be beneficial. IV tecovirimat should be initiated if not already being used, particularly if there are concerns about gastrointestinal absorption (**BIII**). The addition of other therapeutics, including brincidofovir or cidofovir and VIGIV, should also be assessed if they are not already being used. Extending the duration of tecovirimat treatment should be done carefully, through short increments of time (e.g., an additional 3 to 7 days), while monitoring for clinical improvement or lack of response and adverse events to assess continuing or stopping treatment accordingly (**BIII**). Tecovirimat resistance has also been detected in a small number of patients with advanced HIV who received tecovirimat for durations of weeks to months.^{101,102}

Clinicians can send repeat sample swabs to the [CDC](#) to assess for the continued presence of MPXV and for evidence of potential viral resistance based on genetic sequencing (**CIII**). Formal tecovirimat sensitivity testing results cannot be used to guide treatment decisions for individual patients for two reasons: first, they require culture-based resistance testing techniques that take weeks to perform (i.e., results cannot be returned in a timely manner); and second, reporting of these results is not permitted under Clinical Laboratory Improvement Amendments. However, the results of tecovirimat

susceptibility testing are helpful to public health efforts to monitor for the emergence of tecovirimat resistance.

Persistently positive PCR test results are expected until lesions resolve; therefore, subsequent testing of lesion specimens may not be informative unless new lesions or progressive lesions occur after 14 days of tecovirimat treatment. Evaluating trends in MPXV PCR cycle threshold (Ct) values may be informative; Ct values ≥ 35 are generally accepted evidence that replication-competent virus is not present in clinically relevant concentration.¹⁰³ Certain laboratories can test for the presence of viable virus with culture techniques, but these results might not be available in a clinically relevant timeframe.

Other possible reasons for treatment failure include a dysregulated immune response with associated inflammation or the presence of another opportunistic infection. If viable MPXV is still detected by culture, then viral replication and ongoing infection might be driving the disease process and antiviral medications should be continued. Biopsy of the affected tissue can be performed in cases with new or atypical lesions where it is unclear if the lesions are primarily due to mpox or another infectious cause, including secondary bacterial or fungal infections, and in cases with significant complications (e.g., mucosal or bowel lesions, severe lymphadenopathy, pulmonary nodular lesions, severe conjunctivitis). Consultation with infectious disease specialists and the CDC is encouraged.

The use of topical or ablative therapies for progressive hypertrophic lesions has been reported, but their role still remains under exploration.¹⁰⁴ Consultation with an infectious disease specialist, dermatologist, and wound care specialist (or facility) should be sought. The CDC offers a clinical consultation service (email poxvirus@cdc.gov), or health care providers may contact the CDC Emergency Operations Center at 770-488-7100, where the CDC can provide additional guidance to clinicians with patient management questions.

Preventing Recurrence and Reinfection

The durability of immunity after either infection with mpox or vaccination is unknown, including among people with HIV. No clinical correlates of immunity have yet been established to guide when additional vaccination might be needed following infection. Reinfection with mpox remains very rare. Observational data indicate people with acquired immunity after initial infection tend to have a self-limited illness with a lower burden of lesions that can be managed in outpatient settings.^{105,106} Per CDC clinical considerations, people who have recovered from mpox are **not recommended** to receive JYNNEOS vaccine doses.⁷⁰ At this time, additional vaccinations for people with prior mpox and with advanced HIV (CD4 < 200 cells/mm³) following immune reconstitution are **not recommended (CIII)**.

Special Considerations During Pregnancy

Data regarding mpox infection in pregnancy are scant and largely limited to case reports and case series.^{5,52,107-112} Whether pregnant women are more susceptible to mpox or experience more severe disease remains unknown.^{107,113} For considerations related to immunization during pregnancy, please refer to the [Mpox Vaccine section](#) of the Immunization chapter.

Adverse pregnancy outcomes of mpox historically associated with maternal infection include spontaneous pregnancy loss, stillbirth, and preterm delivery.⁵ One meta-analysis synthesized available data from four studies with seven mpox-affected pregnancies prior to 2019 and estimated

the risk for miscarriage was 39% (three pregnancies with 95% confidence interval [CI], 0.00–0.89) and for intrauterine fetal demise 23% (two pregnancies; 95% CI, 0.00–0.74).¹⁰⁹ A subsequent meta-analysis that synthesized data from six studies (two new studies in addition to the four analyzed in the prior meta-analysis) with 12 mpox-affected pregnancies, including pregnancies from the recent outbreak, estimated the risk for fetal death was 50% (95% CI, 27–79).¹¹⁰ Adverse outcomes might differ by MPXV clade, but the data remain sparse. A recent report of eight pregnant women with confirmed clade I mpox infection in the Democratic Republic of the Congo (DRC) found miscarriage in all four women infected during the first trimester.¹¹⁴ *In utero* transmission of clade I mpox infection has also been reported. A 21-week stillborn fetus born to a woman with confirmed clade I mpox infection from the DRC showed cutaneous maculopapular lesions, with viral DNA identified in both fetal and placental tissues, confirming *in utero* transmission.⁵

In contrast, during the 2022 to 2023 clade II mpox outbreak, there were no reports of maternal death or intrauterine infection, and adverse pregnancy outcomes (e.g., pregnancy loss) were less common.^{52,111,112} These findings suggest that the clade II infection might be associated with a lower risk of adverse perinatal outcomes than the clade I infection.

The signs and symptoms of mpox infection in pregnant women appear similar to those in nonpregnant women, including prodromal symptoms and rash. The approach to diagnosis of mpox in pregnant women is the same as in nonpregnant women.

Because pregnancy represents an immunosuppressed state and vertical transmission of mpox has been documented, treatment for mpox should be offered to women who are pregnant, recently pregnant, or breastfeeding (**AIII**). Tecovirimat is available through CDC-sponsored [EA-IND](#) for women who are pregnant or breastfeeding. No adverse reactions were reported in a small series of pregnant women who received tecovirimat.¹¹¹ Information about the impact of tecovirimat on reproductive development is limited to animal studies in which no specific fetal effects were observed.⁷⁹ It is not known if treatment with tecovirimat during pregnancy prevents congenital mpox, and reports of its use during 12 human pregnancies described no harmful effects.¹¹⁵ Animal reproduction studies have not been conducted with VIGIV; therefore, it is not known whether VIGIV can cause fetal harm when administered during pregnancy or can affect future fertility.⁸⁸ However, other immune globulins have been widely used during pregnancy for many years without any apparent negative reproductive effects. In animal studies, cidofovir and brincidofovir have been shown to be teratogenic; therefore, these agents are **not recommended** for use in pregnancy (**AIII**).^{97,98}

Considerations for mpox and breastfeeding are complex and should be discussed with the patient using shared decision-making. For additional information, see [Mpox Clinical Care and Treatment During Pregnancy](#).

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