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CDC HEALTH ADVISORY

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Severe Manifestations of Monkeypox among People who are Immunocompromised Due to HIV or Other Conditions

Summary

The purpose of this Centers for Disease Control and Prevention (CDC) Health Alert Network (HAN) Health Advisory is to inform healthcare providers that

- 1) Severe manifestations of monkeypox have been observed in the United States in the current outbreak.
- 2) People who are immunocompromised due to HIV or other conditions are at higher risk for severe manifestations of monkeypox than people who are immunocompetent.
- 3) Because people with HIV-associated immunocompromise are at risk for severe manifestations of monkeypox, the HIV status of all sexually active adults and adolescents with suspected or confirmed monkeypox should be determined.
- 4) There are diagnostic and clinical management strategies that may help address severe manifestations of monkeypox.

Background

Since May 2022, more than 25,000 [monkeypox cases](#) have been identified in the United States. During the current outbreak in the United States, 38 percent of people diagnosed with monkeypox were coinfecting with HIV¹ and most reported cases of monkeypox with severe manifestations have been among people living with untreated HIV.

Some patients with monkeypox in the United States have experienced prolonged hospitalizations or substantial morbidity; deaths have occurred. As the monkeypox outbreak has progressed, an increasing proportion of cases have been identified among Black and Hispanic/Latino people. Black and Hispanic/Latino people are disproportionately affected by HIV.

Severe manifestations of monkeypox can occur in both immunocompetent and immunocompromised people; however, most people diagnosed with monkeypox have had mild-to-moderate clinical courses. Of the people with severe manifestations of monkeypox for whom CDC has been consulted, the majority have had HIV with CD4 counts <200 cells/ml, indicating substantial immunosuppression. Healthcare providers should recognize underlying risk factors for severe disease, optimize immune function, and when appropriate, initiate medical countermeasures (such as tecovirimat and vaccinia immunoglobulin) early to prevent or mitigate severe disease.

During the current outbreak, CDC has received reports of people with monkeypox who have severe manifestations of disease, including but not limited to

- Atypical or persistent rash with coalescing or necrotic lesions, or both, some which have required extensive surgical debridement or amputation of an affected extremity.
- Lesions on a significant proportion of the total body surface area, which may be associated with edema and secondary bacterial or fungal infections among other complications.
- Lesions in sensitive areas (including mucosal surfaces such as, oropharynx, urethra, rectum, vagina) resulting in severe pain that interferes with activities of daily living.
- Bowel lesions that are exudative or cause significant tissue edema, leading to obstruction.
- Severe lymphadenopathy that can be necrotizing or obstructing (such as in airways).

- Lesions leading to stricture and scar formation resulting in significant morbidity such as urethral and bowel strictures, phimosis, and facial scarring.
- Involvement of multiple organ systems and associated comorbidities, including:
 - Oropharyngeal lesions inhibiting oral intake
 - Pulmonary involvement with nodular lesions
 - Neurologic conditions including encephalitis and transverse myelitis
 - Cardiac complications including myocarditis and pericardial disease
 - Ocular conditions including severe conjunctivitis and sight-threatening corneal ulcerations
 - Urologic involvement including urethritis and penile necrosis

Healthcare providers should be aware of risk factors for severe manifestations of monkeypox and should conduct HIV testing for people with confirmed or suspected monkeypox. In prior monkeypox outbreaks in Nigeria, co-infection with HIV was associated with worse clinical outcomes, including severe manifestations of monkeypox, hospitalization, and death.² Providers should also consider other [immunocompromising conditions](#)* and medications that may increase risk of severe manifestation of monkeypox.

In immunocompromised people, monkeypox treatment should include optimizing immune function by limiting the use of immunosuppressive medications if not otherwise clinically indicated, and, for those with HIV, providing antiretroviral therapy. In addition, there are medical countermeasures that may have a role in treating severe illness, including oral and intravenous tecovirimat (TPOXX), cidofovir or brincidofovir, and vaccinia immune globulin intravenous (VIGIV), although there are no data on effectiveness in treating human monkeypox with these medical countermeasures. Decisions on whether and when to use these medical countermeasures must be made individually for each person and can depend on a variety of clinical and other parameters.

Healthcare providers of people with monkeypox who are at risk for or who have severe manifestations of disease should reach out to their local public health jurisdictions or CDC for guidance about appropriate treatment. People with severe manifestations of monkeypox may benefit from multidisciplinary consultation with specialists such as infectious disease, ophthalmology, dermatology, urology, or critical care medicine. CDC offers a clinical consultation service (email eocevent482@cdc.gov or healthcare providers may contact the CDC Emergency Operations Center [EOC] at (770) 488-7100) and can provide additional guidance to clinicians with patient management questions. Clinicians seeking treatments should work with their local or state public health jurisdictions and CDC to access appropriate treatments as soon as potential need becomes apparent.

Worsening, non-healing, recurrent, and new skin lesions while receiving antiviral treatment have been observed among immunocompromised people with severe manifestations of monkeypox. Clinicians are encouraged to obtain repeat lesion swabs to assess for persistent monkeypox DNA. In such people, clinicians may consider continuing tecovirimat beyond 14 days, until there is clinical improvement (no more than 90 days).³ In certain clinical situations, modifications to the dose, frequency, and duration may be necessary depending on the individual patient's clinical condition, disease progression, therapeutic response, and/or clinical judgement in consultation with CDC and U.S. Food and Drug Administration (FDA) as appropriate. To request clinical consultation regarding dosing adjustments, contact the CDC EOC at (770) 488-7100 or send an email to eocevent482@cdc.gov.³

Currently, CDC is conducting surveillance to monitor for the development of resistance to tecovirimat primarily from specimens that were sent to CDC for monkeypox confirmatory testing; however, resistance testing results are not CLIA-waived (approved) for use in clinical decision making. For the purposes of public health surveillance, CDC encourages clinicians to submit specimens for further monkeypox virus characterization through genetic sequencing to identify mutations that could potentially result in resistance to antiviral therapy. At this time, after evaluating more than 600 samples, there have been no specimens with mutations associated with tecovirimat resistance; however, it is not clear how many of those samples were collected from people with disease progression while on tecovirimat.

*Severe immunocompromise due to leukemia, lymphoma, generalized malignancy, solid organ transplantation, therapy with alkylating agents, antimetabolites, radiation, tumor necrosis factor inhibitors, or high-dose corticosteroids, being a recipient of a hematopoietic stem cell transplant <24 months post-transplant or ≥24 months but with graft-versus-host disease or disease relapse, or having autoimmune disease with immunodeficiency as a clinical component

Recommendations for Healthcare Providers

- Upon initial presentation of signs and symptoms consistent with monkeypox, in addition to monkeypox, test all sexually active adults and adolescents for HIV (including acute infection) and other sexually transmitted infections (such as syphilis, herpes, gonorrhea, and chlamydia), and assess for other immunocompromising conditions.*
- Be familiar with severe manifestations of monkeypox and risk factors for severe disease.
- Contact local and state health departments early when there is concern for progression to severe manifestations or severe manifestations are present for guidance on management and securing necessary resources for treatment.
- Consider treating immunocompromised people diagnosed with monkeypox with tecovirimat early in the course of disease and consider a prolonged course of tecovirimat for those with more refractory and severe monkeypox infection. In certain clinical situations, modifications to the dose, frequency, and duration may be necessary depending on the individual's clinical condition, disease progression, therapeutic response, and clinical judgement in consultation with CDC and FDA as appropriate. To request clinical consultation regarding dosing adjustments, contact the CDC EOC at (770) 488-7100 or send an email to eocevent482@cdc.gov.
- Where available, healthcare providers should encourage people with monkeypox to be assessed for enrollment in the [ACTG STOMP trial](#) evaluating the efficacy of [tecovirimat](#).
- Have a low threshold to use multiple medical countermeasures, including tecovirimat, cidofovir or brincidofovir, and VIGIV in immunocompromised people who present with severe manifestations of monkeypox or are at high risk of progression to severe manifestations.
- Optimize immune function among immunocompromised people with suspected or confirmed monkeypox, specifically by ensuring those with HIV are on effective antiretroviral therapy.
- Discuss [HIV pre-exposure prophylaxis \(PrEP\)](#) with those who are HIV negative and at risk for HIV.
- Consider consultation with CDC Monkeypox Response Clinical Escalations Team (email eocevent482@cdc.gov or healthcare providers may contact the CDC EOC at (770) 488-7100), and multidisciplinary consultation with specialists such as infectious disease, ophthalmology, dermatology, urology, or critical care medicine.

Recommendations for Public Health Jurisdictions

- Facilitate and encourage testing for monkeypox, HIV, and other sexually transmitted infections in every sexually active adult and adolescent in whom monkeypox is suspected.
- Provide educational resources to clinicians on severe manifestations of monkeypox.
- Provide guidance to clinicians on diagnosing and treating monkeypox, including severe manifestations of monkeypox.
- Encourage health care providers to refer people with monkeypox to be assessed for enrollment in the [ACTG STOMP trial](#) evaluating the efficacy of tecovirimat.
- Facilitate easy and quick access to monkeypox medical countermeasures across jurisdictions.
- Facilitate access to HIV PrEP for those who are eligible and linkages to care and antiretroviral therapy for those with HIV.
- Contact CDC Monkeypox Response Clinical Escalations Team (email eocevent482@cdc.gov or contact the CDC Emergency Operations Center (EOC) at (770) 488-7100) as needed for access to treatment or guidance on how and when to administer different monkeypox treatment options.

Recommendations and Information for the Public

- If you think you have monkeypox or have had close personal contact with someone who has monkeypox, [visit a healthcare provider](#) to help decide if you need to be tested for monkeypox or would benefit from vaccination. Currently, testing is only recommended if you have a rash consistent with monkeypox.
- If you were exposed to monkeypox through sexual contact, you should also be tested for HIV and other sexually transmitted infections.
- If your monkeypox test result is positive, take the [necessary steps](#) to protect yourself and others until you have completely recovered from your infection.
- There are no treatments specifically for monkeypox. But because the viruses that cause monkeypox and smallpox are similar, antiviral drugs developed to protect against smallpox may be used to treat monkeypox effectively.
- The [antiviral drug tecovirimat](#) (TPOXX) has been made available by the FDA through an expanded access investigational new drug protocol to treat monkeypox in adults and children.
- TPOXX is currently recommended for people with severe monkeypox disease or who are at high risk of severe disease, like people with weakened immune systems, such as HIV that is not virally suppressed, or skin conditions, such as eczema.
- If you are someone with a weakened immune system or are living with HIV and have been exposed to monkeypox or developed an illness or rash consistent with monkeypox, you should seek out testing and treatment for monkeypox from a healthcare provider.

References

1. HIV and Sexually Transmitted Infections Among Persons with Monkeypox—Eight U.S. Jurisdictions, May 17–July 22, 2022. *MMWR Morb Mort Wkly Rep* 2022; 71(36):1141 – 1147. <https://www.cdc.gov/mmwr/volumes/71/wr/mm7136a1.htm>
2. Outbreak of Human Monkeypox in Nigeria in 2017–18: A Clinical and Epidemiological Report – *The Lancet Infectious Diseases*. [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(19\)30294-4/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(19)30294-4/fulltext)
3. Centers for Disease Control and Prevention. Expanded Access IND Protocol: Use of Tecovirimat (TPOXX) for Treatment of Human Non-Variola Orthopoxvirus Infections in Adults and Children (IND 116,039/Protocol #6402). <https://www.cdc.gov/poxvirus/monkeypox/clinicians/obtaining-tecovirimat.html>

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