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Antiviral Considerations for Monkeypox Infection – USE CAUTION!

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This month, the United States Food and Drug Administration (FDA) issued a warning regarding antiviral use for monkeypox (MPX) infection. Concomitant with rising numbers of cases worldwide, MPX appears to be rapidly mutating with indications of emerging resistance to antiviral therapy. To slow the mutation, the FDA is advising care providers to use antivirals judiciously and only for serious expressions of MPX infection.[1]

The antiviral tecovirimat, brand name TPOXX or ST-246, is approved for the treatment of human smallpox caused by the variola virus. It is NOT approved by the FDA for other types of orthopoxvirus infections such as MPX. Since there is no antiviral specific for MPX, tecovirimat is available through a randomized controlled clinical trial sponsored by the National Institutes of Allergy and Infectious Diseases (NIAID) and through the Centers for Disease Control and Prevention (CDC) under the FDA authority granting expanded access or "compassionate use" for MPX.[2] This approval in 2018 was based on efficacy data from nonhuman primates infected with monkeypox and safety data obtained from healthy volunteer human subjects with no infection. The efficacy and safety of tecovirimat in treating humans with MPX infection are unknown.[1]

Tecovirimat inhibits the VP37 protein which all orthopoxviruses (smallpox, monkeypox, vaccinia virus) share. Data suggest that the monkeypox virus may be moving toward a modified viral structure without VP37 proteins, which would render tecovirimat ineffective, particularly since tecovirimat has a low barrier to viral resistance. What this means is that small changes to the VP37 protein may have a large impact on the antiviral activity of tecovirimat. The FDA acknowledges multiple independent reports that have identified the development of antiviral resistance to tecovirimat in cell culture and animal studies and amino acid substitutions that reduce tecovirimat antiviral activity. In summary, there is increasing anxiety that a tecovirimat-resistant virus will emerge and spread quickly.[1]

The CDC now recommends that tecovirimat should not be prescribed to otherwise healthy adults with low symptom burden in MPX infection. Care providers who desire to prescribe tecovirimat must submit an application to CDC requesting tecovirimat and must agree to track and report outcomes as well as side effects with use. Tecovirimat is available from the US national stockpile for bioterrorism attack response.[1] Clinicians can also direct patients to possibly participate in a clinical trial that started on September 8, 2022, to establish the safety and efficacy of tecovirimat in human monkeypox infection, viral mutation, and development of resistance.[1,3]

Since broad use of tecovirimat in monkeypox could also result in attenuation of this antiviral treatment for other types of orthopoxvirus infections, careful examination of the risks and benefits of antiviral treatment in MPX is necessary. Before prescribing, consider the efficacy of tecovirimat, particularly with the current lack of evidence regarding who is most likely to benefit from therapy and the risks for the development of resistance.[4]

For patients at high risk for severe disease, tecovirimat should be started early in the infection concomitant with supportive care and pain control. Table describes when tecovirimat should be considered for use in MPX infection.[5] For emergencies after hours, contact CDC Emergency Operations Center at 770-488-7100 for information and clinical consultation.[2,6] Patients ineligible for tecovirimat treatment under the CDC and FDA *expanded access investigational new drug* (EA-IND) process include patients (or their legally authorized representatives) who are unwilling to sign an informed consent, refuse tecovirimat treatment, or patients with known allergy to tecovirimat and/or inactive ingredients of tecovirimat formulation.[4,5]

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Table. Current Considerations for Use of Tecovirimat in Monkeypox Infection[4]

Severe Disease Expression
○ Hemorrhagic disease
○ Confluent lesions
○ Sepsis or encephalitis
○ Ocular or periorbital infection
○ Required hospitalization
Risk for Scarring/Stricture — Anatomic Locations of Lesions
○ Lesions of the pharynx with dysphagia
○ Inability to control secretions
○ Parenteral feeding required
○ Penile foreskin, vulva, vagina, urethra, or rectum
○ Restriction of bowel movements, severe pain with bowel movements
○ Severe bacterial infections
○ Surgical debridement required
Persons with High Risk for Disease
○ Advanced/poorly controlled human immunodeficiency virus infection
○ Leukemia, lymphoma, generalized malignancy
○ Solid organ transplant
○ Receiving therapy: alkylating agents, antimetabolites, radiation, tumor necrosis factor inhibitors
○ Receiving high-dose corticosteroids
○ Hematopoietic stem cell transplant (< 24 months post-transplant or > 24 months with graft-versus-host disease or disease relapse)
○ Autoimmune disease with immunodeficiency
○ Pediatric populations especially patients younger than 8 years
○ Pregnant or breastfeeding
○ Atopic dermatitis, eczema, burns, impetigo, psoriasis
○ Varicella zoster virus infection
○ Herpes simplex virus infection
○ Severe acne, severe diaper dermatitis with extensive areas of denuded skin
○ Darier disease

The NIAID tecovirimat research protocol is available on the CDC website, and treatment can begin upon receipt of tecovirimat and obtaining informed consent.[5,6] This phase 3 double-blind clinical trial will evaluate tecovirimat in children and adults with MPX infection in the United States. Adults with severe infection as well as those at high risk for severe disease will be enrolled in an open-label arm in which all participants receive tecovirimat. Other adult participants (530 total) will be randomly assigned in a 2:1 ratio to receive tecovirimat or placebo. Tecovirimat capsules are taken by mouth for 14 days, and the dose is weight-based. For this part of the trial, neither subjects nor investigators will know who is receiving placebo or tecovirimat. Study goals include determining if tecovirimat is associated with faster healing of lesions, reduced pain, and improved viral clearance, as well as safety and optimal dosing for children and pregnant women. An independent data and safety monitoring board will monitor subject safety during the study, and findings related to safety and efficacy will be submitted to the FDA.[4,6,7]

References

1. US Food and Drug Administration. FDA monkeypox response. https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/fda-monkeypox-response#therapeutics. Current September 15, 2022. Accessed September 19, 2022.
2. Centers for Disease Control and Prevention. Information for healthcare providers on obtaining and using TPOXX (tecovirimat) for treatment of monkeypox. https://www.cdc.gov/poxvirus/monkeypox/clinicians/obtaining-tecovirimat.html. Updated September 2, 2022. Accessed September 19, 2022.
3. AIDS Clinical Trials Group (ACTG). A5418: study of tecovirimat for human monkeypox virus (STOMP). https://actgnetwork.org/studies/a5418-study-of-tecovirimat-for-human-monkeypox-virus-stomp/. Accessed September 19, 2022.
4. Centers for Disease Control and Prevention. Guidance for tecovirimat use under expanded access investigational new drug protocol during 2022 U.S. monkeypox outbreak. https://www.cdc.gov/poxvirus/monkeypox/clinicians/Tecovirimat.html. Updated September 15, 2022. Accessed September 19, 2022.
5. Centers for Disease Control and Prevention. Treatment information for healthcare professionals. https://www.cdc.gov/poxvirus/monkeypox/clinicians/treatment.html. Updated September 15, 2022. Accessed September 19, 2022.
6. 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 no. 116,039 CDC IRB no. 6402 version 6.1. https://www.cdc.gov/poxvirus/monkeypox/pdf/Tecovirimat-IND-Protocol-CDC-IRB.pdf. August 10, 2022. Accessed September 19, 2022.
7. National Institute of Allergy and Infectious Diseases (NIAID). U.S. clinical trial evaluating antiviral for monkeypox begins. NIH trial gathering data on tecovirimat (TPOXX). https://www.niaid.nih.gov/news-events/us-clinical-trial-evaluating-antiviral-monkeypox-begins. September 9, 2022. Accessed September 20, 2022.

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