Centers for Disease Control and Prevention

Monkeypox

Guidance for Tecovirimat Use Under Expanded Access Investigational New Drug Protocol during 2022 U.S. Monkeypox Outbreak

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Tecovirimat (also known as TPOXX or ST-246) is FDA-approved for the treatment of human smallpox disease caused by *Variola virus* in adults and children. However, its use for other orthopoxvirus infections, including monkeypox, is not approved by the FDA. Therefore, CDC holds a non-research expanded access Investigational New Drug (EA-IND) protocol (sometimes called "compassionate use") that allows for the use of tecovirimat for primary or early empiric treatment of non-variola orthopoxvirus infections, including monkeypox, in adults and children of all ages. Tecovirimat use allowed under the EA-IND protocol [1 MB, 22 pages] is intended to be used in concert with CDC guidance for treatment of monkeypox. Tecovirimat is available from the Strategic National Stockpile and is provided at no cost.

Learn about how to obtain tecovirimat and the requirements under the EA-IND protocol.

Learn about the National Institutes of Health (NIH)-funded clinical trial of tecovirimat.

Treatment Considerations

The ongoing monkeypox outbreak in the United States is caused by Clade IIb of the monkeypox virus. Patients with monkeypox benefit from supportive care and pain control that is implemented early in the illness (Clinical Considerations for Pain Management of Monkeypox). Illness depends on a person's immune response. For most patients with intact immune systems, supportive care and pain control may be enough. However, because prognosis depends on multiple factors, such as initial health status, concurrent illnesses, previous vaccination history, and comorbidities, supportive care and pain control may not be enough for some patients (for example, those with weakened immune systems). Tecovirimat should be considered for those patients.

Data on the effectiveness of tecovirimat in treating people with monkeypox are not available but studies using a variety of animal species have shown that tecovirimat is effective in treating disease caused by orthopoxviruses. In animal studies, tecovirimat has been shown to decrease the chance of dying from infections with orthopoxviruses when given early in the disease course. A clinical trial that focused on safety in healthy people without monkeypox virus infection showed the drug had an acceptable safety profile; the effectiveness of tecovirimat was not studied in this trial.

Data from the published literature and additional recently released data from the U.S. Food and Drug Administration suggest that there may be a low barrier to virus developing resistance to tecovirimat; indiscriminate use could promote resistance and render tecovirimat, first line treatment for orthopoxviruses, ineffective for patients. Alternate therapeutics have more concerning safety profiles than tecovirimat.

When considering the use of tecovirimat, clinicians and patients should understand 1) the lack of tecovirimat effectiveness data to date in people with monkeypox, 2) the lack of data indicating which patients might benefit the most from tecovirimat, and 3) the concern for the development of resistance to tecovirimat, which could render the drug ineffective for any treated patients.

Tecovirimat should be considered for use in people who have the following clinical manifestations:

- Severe disease — consider severe disease when a patient has conditions such as hemorrhagic disease; large number of lesions such that they are confluent; sepsis; encephalitis; ocular or periorbital infections; or other conditions requiring hospitalization
- Involvement of anatomic areas which might result in serious sequelae that include scarring or strictures — these include lesions directly involving the pharynx causing dysphagia, inability to control secretions, or need for parenteral feeding; penile foreskin, vulva, vagina, urethra, or rectum with the potential for causing strictures or requiring catheterization; anal lesions interfering with bowel movements (for example, severe pain); and severe infections (including secondary bacterial skin infections), especially those that require surgical intervention such as debridement

Tecovirimat should also be considered for use in people who are at high risk for severe disease:

- People currently experiencing severe immunocompromise due to conditions such as advanced or poorly controlled human immunodeficiency virus (HIV), 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[1]
- Pediatric populations, particularly patients younger than 8 years of age[2]
- Pregnant or breastfeeding people[3]
- People with a condition affecting skin integrity — conditions such as atopic dermatitis, eczema, burns, impetigo, varicella zoster virus infection, herpes simplex virus infection, severe acne, severe diaper dermatitis with extensive areas of denuded skin, psoriasis, or Darier disease (keratosis follicularis)

For patients at high risk for progression to severe disease, tecovirimat should be administered early in the course of illness along with supportive care and pain control.

> More Information: Treatment Information for Healthcare Professionals

People who are ineligible for tecovirimat treatment under the EA-IND include:

- Patients (or their legally authorized representatives) who are unwilling to sign an informed consent and refuse tecovirimat treatment
- Patients with known allergy to tecovirimat and/or inactive ingredients of tecovirimat formulation

Available Formulations

Tecovirimat is available as an oral capsule (200 mg) and injection for intravenous (IV) administration. Drug absorption of oral formulation is dependent on adequate concurrent intake of a full, fatty meal.

IV tecovirimat should not be administered to patients with severe renal impairment (CrCl <30mL/min). Oral formulation remains an option for this population. IV tecovirimat should be used with caution in patients with moderate (CrCl 30-49 mL/min) or mild (CrCl 50-80 mL/min) renal impairment as well as in pediatric patients < 2 years of age given immature renal tubular function.

Adverse Reactions

- Oral: headache (12%), nausea (5%), abdominal pain (2%), and vomiting (2%). Neutropenia was found in one study participant.
- IV: infusion site pain (73%), infusion site swelling (39%), infusion site erythema (23%), infusion site extravasation (19%), and headache (15%).

Drug-Drug Interactions

Significant interactions have been reported in healthy adults with co-administration of repaglinide (hypoglycemia) and midazolam (decreased effectiveness of midazolam).

Special Populations

Pregnancy/Lactation

Although tecovirimat has not been studied in pregnant and nursing women, they are not excluded from treatment if deemed appropriate following careful clinical assessment and discussion of risks/benefits with patient using a shared decision-making model. There are no human data to establish the presence or absence of tecovirimat-associated risk of fetotoxicity, effect on milk production, the presence of drug in human milk, and/or effects on breastfed children. No fetotoxicity was found in animal studies, though tecovirimat was detected in trace amounts in milk.

Pediatrics

Tecovirimat has been used in a 28-month-old child with no adverse effects attributed to the drug, but no clinical studies have been done in pediatric populations. Monitoring of renal function is recommended in pediatric patients <2 years of age, given theoretical concerns that renal immaturity in young pediatric patients may result in higher exposure of hydroxypropyl-β-cyclodextrin, an ingredient in IV tecovirimat. Animal studies have shown potential for nephrotoxicity at very high exposure levels of hydroxypropyl-β-cyclodextrin.

References

1. Ogoina D, Iroezindu M, James HI, Oladokun R, Yinka-Ogunleye A, Wakama P, Otike-Odibi B, Usman LM, Obazee E, Aruna O, Ihekweazu C. Clinical Course and Outcome of Human Monkeypox in Nigeria. Clin Infect Dis. 2020 Nov 5;71(8):e210-e214. doi: 10.1093/cid/ciaa143. PMID: 32052029.
2. Jezek Z, Szczeniowski M, Paluku KM, Mutombo M. Human monkeypox: clinical features of 282 patients. J Infect Dis. 1987 Aug;156(2):293-8. doi: 10.1093/infdis/156.2.293. PMID: 3036967.
3. Mbala PK, Huggins JW, Riu-Rovira T, Ahuka SM, Mulembakani P, Rimoin AW, Martin JW, Muyembe JT. Maternal and Fetal Outcomes Among Pregnant Women With Human Monkeypox Infection in the Democratic Republic of Congo. J Infect Dis. 2017 Oct 17;216(7):824-828. doi: 10.1093/infdis/jix260. PMID: 29029147.

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