Tecovirimat (TPOXX) Frequently Asked Questions
October 27, 2022

1. **What is tecovirimat (TPOXX) and how is it taken?**
    - TPOXX is an antiviral drug approved by the FDA in 2018 to treat smallpox in adults and children.
    - TPOXX is available in capsule form (each capsule contains 200 mg of tecovirimat) and as an intravenous (IV) solution. TPOXX capsules are used much more often than the IV preparation. The dosage of TPOXX is determined by the patient's weight. Please see the TPOXX prescribing information for recommended dosing and administration instructions. TPOXX capsules should be taken within 30 minutes after a full meal of moderate or high fat. Treatment duration is typically 14 days but may be longer (not to exceed 90 days) or shorter depending on the progression of the disease and clinical condition of the patient. Data on duration other than 14 days are limited.

2. **Are there any FDA-approved treatments for monkeypox virus infection and why is TPOXX being used for monkeypox if it hasn't been approved by the FDA?**
    - There are currently no FDA-approved treatments for monkeypox virus infections.
    - CDC holds a non-research Expanded Access Investigational New Drug (EA-IND, also known as compassionate use) protocol that allows TPOXX to be used for treatment of monkeypox virus in children and adults.

3. **Who should TPOXX be used for and are there circumstances in which TPOXX should not be used?**
    - Treatment with TPOXX should be considered in patients with severe monkeypox disease. Severe disease includes conditions such as a large number of skin lesions such that they are confluent, sepsis, encephalitis, ocular or periorbital infections, or other conditions requiring hospitalization. Patients with monkeypox disease that involves anatomic areas where scarring or stricture formation (e.g., urethra, bowel, anorectal area) may result in serious sequelae should be considered for TPOXX therapy.
    - Treatment with TPOXX should also be considered for patients who are at high-risk of progression to severe monkeypox disease. This would include patients who are immunocompromised from any cause (e.g., HIV/AIDS, cancer, status post organ transplantation, medication that suppresses immune function). Pediatric patients, particularly children less than 8 years old, pregnant or breastfeeding people, and patients with conditions affecting skin integrity such as burns, atopic dermatitis, herpes simplex virus infection and other skin diseases are also considered at high-risk for severe monkeypox.
    - Patients (or their legally authorized representatives) who should not receive TPOXX include: those unwilling to provide consent or otherwise refuse the

treatment, those with a known allergy to tecovirimat and/or inactive ingredients in the drug formulation.

- For those patients for whom TPOXX is recommended, early administration is best. Patients can begin treatment as soon as they have provided informed consent to their healthcare provider, and the provider is enrolled in the Expanded Access Investigational New Drug (EA-IND) protocol.
- Of note, The National Institute of Allergy and Infectious Diseases, part of the U.S. National Institutes of Health, has a clinical trial underway for the antiviral drug TPOXX. The trial, Study of Tecovirimat for Human Monkeypox Virus (STOMP), is enrolling adults and children of any age with monkeypox infection at 80 clinical research sites in the United States.

4. **Can TPOXX be used in pregnant or breastfeeding patients?**
   CDC recommends prioritizing treatment of pregnant and breastfeeding women with monkeypox with TPOXX since they are at higher risk of complications from the disease. More information about monkeypox in pregnancy and breastfeeding can be found at CDC Clinical Considerations for Monkeypox in People Who are Pregnant or Breastfeeding.

5. **What are possible adverse effects of oral TPOXX and is there data showing the effectiveness of TPOXX in people with monkeypox?**
   - Possible adverse effects of oral TPOXX include, but are not limited to: headache (12%), nausea (5%), abdominal pain (2%), and vomiting (2%).
   - Possible adverse effects of IV TPOXX include, but are not limited to: injection site reactions (19%-73%) and headache (15%).
   - Other adverse reactions, drug interactions, and special population considerations (pregnancy/lactation and pediatrics) can be found on the CDC's Interim Clinical Guidance for the Treatment of Monkeypox.
   - Currently, there is no data establishing safety or effectiveness using TPOXX to treat monkeypox in humans.

6. **What documentation is required for healthcare providers to complete in order to obtain TPOXX and what are the requirements for TPOXX prescribing/initiating?**
   - Clinicians interested in prescribing TPOXX for the treatment of monkeypox should review the CDC requirements and CDC attestation. Clinicians wishing to initiate treatment for monkeypox should be prepared to complete the following documentation:
     - FDA Form 1572: One signed 1572 per facility suffices for all tecovirimat treatments administered under the EA-IND at the same facility.
     - Informed Consent Form
     - Patient Intake Form
     - Adverse Event Form: Life-threatening or serious adverse events associated with TPOXX use should be reported to CDC

(regaffairs@cdc.gov) within 24 hours of occurrence, or as soon as possible.

- These forms must be emailed directly to the CDC at regaffairs@cdc.gov within 7 days of treatment initiation.
- Additionally, medical providers must report wastage, administration, and inventory to VDH via the TPOXX Inventory & Patient Initiation Survey for all patients who are started on TPOXX.

The CDC holds an intermediate-size patient population EA-IND (IND 116,039/Protocol 6402) to allow access to and use of TPOXX for orthopoxvirus infections, including monkeypox. The EA-IND provides an umbrella regulatory coverage so that clinicians and facilities do not need to request and obtain their own INDs. The EA-IND also provides liability coverage under the PREP Act for compensation to patients if injured via the Countermeasure Injury Compensation Program (CICP).

7. **How do healthcare providers request and obtain TPOXX, and who should they contact for more information or questions about TPOXX?**
    - In order to begin providing TPOXX or prepositioning TPOXX at your facility, complete the TPOXX Provider Treatment Initiation Interest Form and VDH will review and ship orders directly to the provider.
    - TPOXX is available through the CDC's Strategic National Stockpile (SNS). **To request TPOXX, clinicians must complete the TPOXX Provider Treatment Initiation Interest Form**. Providers requesting TPOXX for an identified patient will have the following choices for medication distribution:
        1. VDH dispenses the medication and ships the medication directly to the patient
        2. VDH dispenses the medication and ships the medication to the provider for the provider to give to the patient

      VDH distributes the medication to the provider and the provider dispenses (i.e. labels the medication). The provider may then give the medication to the patient. *Please note this option is only for providers that can dispense medication consistent with the Virginia Board of Pharmacy regulations.
    - Local health departments, infectious disease providers and health systems may also request additional TPOXX supply to have prepositioned for expedited time to treatment. Prepositioned inventory requests will be fulfilled based on TPOXX inventory and disease burden.
    - Please contact the Virginia Department of Health (VDH) at mpxquestions@vdh.virginia.gov if you have additional questions or require further guidance and/or assistance.
    - Additional resources:
        - https://www.fda.gov/media/160480/download
        - https://aspr.hhs.gov/monkeypox/TPOXXOperationalGuidance/Pages/TPOXX-tecovirimat.aspx

- https://www.cdc.gov/poxvirus/monkeypox/clinicians/Tecovirimat.html
- https://www.siga.com/wp-content/themes/sigahba/TPOXX-Fact-Sheet.pdf

8. **Is it possible for a patient to develop resistance to TPOXX and what should a provider do if a patient does not respond to TPOXX?**
    - Data from the published literature and additional recently released data from the FDA suggest that there may be a low barrier to the virus developing resistance to tecovirimat; indiscriminate use could promote resistance and render tecovirimat, first line treatment for orthopoxviruses, ineffective for patients.
    - The possibility of resistance to TPOXX should be considered in patients who either fail to respond to therapy or who develop recurrence of disease after an initial period of responsiveness. To improve our understanding of any resistance that may be occurring, it is critical that viral specimens are obtained from patients that do not respond to treatment so that testing can be completed. Clinicians who would like help with the treatment or management of patients with monkeypox can call the CDC Clinical Consultation service at 770-488-7100 for assistance.

9. **Can I charge my patient for TPOXX or testing services?**
    - At this time, TPOXX should be provided at no cost.
    - There is no funding available to assist with laboratory testing for monkeypox diagnosis. Testing plasma PK samples collected and sent by the hospital to the lab contracted to test PK samples and/or blood or specimens sent via the health department to CDC for serology or virologic testing would not have a cost to the patient.