Obtaining and Using TPOXX (Tecovirimat) for Treatment of Monkeypox

By Raghav Tirupathi MD FACP FIDSA
Monkeppox Facts

- The Monkeypox virus has rapidly spread across the US and the globe
- It has been declared a public health emergency in the USA
- The WHO has declared it a Public Health Emergency of International Concern
- Monkeypox spreads primarily through close and intimate contact
- It can affect people of any age, gender, or race
- The 2022 outbreak in the USA has disproportionately affected gay, bisexual, and other men who have sex with men
- There is a distinct lack of proven, effective and safe treatments
- TPOXX (Tecovirimat) is a promising potential option
Tecovirimat

- There is a theoretical basis for tecovirimat improving outcomes in monkeypox
- There is also anecdotal evidence of tecovirimat speeding up resolution of some symptoms
- However, evidence is sparse and there is an urgent need for clinical trials.
- Despite the endemicity of monkeypox in West Africa, tecovirimat trials have not been conducted to date
- Tecovirimat is approved for smallpox based on studies of primates infected with monkeypox virus*
- NIAID plans to conduct clinical trials beginning Sept 2022 on tecovirimat as a treatment for monkeypox

*The approval was based on the “animal” rule that allows efficacy of drugs for certain life-threatening conditions to be established based on well-controlled studies in animal models of the human disease or condition of interest WHEN it is NOT feasible or ethical to conduct human trials
Indications for TPOXX:

• excruciating anogenital or oral lesions
• immunocompromising conditions
• encephalitis
• eye involvement
• untreated HIV
• atopic dermatitis

Treatment Consideration

Tecovirimat may be considered for treatment in people infected with *Monkeypox virus*:

• With severe disease (e.g., hemorrhagic disease, confluent lesions, sepsis, encephalitis, or other conditions requiring hospitalization)
• Who are at high risk of severe disease:
  ○ People with immunocompromising conditions (e.g., HIV/AIDS, leukemia, lymphoma, generalized malignancy, solid organ transplantation, therapy with alkylating agents, antimetabolites, radiation, tumor necrosis factor inhibitors, high-dose corticosteroids, being a recipient with 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)
  ○ Pediatric populations, particularly patients younger than 8 years of age
  ○ Pregnant or breastfeeding women
  ○ People with a history or presence of atopic dermatitis, people with other active exfoliative skin conditions (e.g., 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])
  ○ People with one or more complication (e.g., secondary bacterial skin infection; gastroenteritis with severe nausea/vomiting, diarrhea, or dehydration; bronchopneumonia; concurrent disease or other comorbidities)
• With aberrant infections involving accidental implantation in eyes, mouth, or other anatomic areas where *Monkeypox virus* infection might constitute a special hazard (e.g., the genitals or anus)
How to obtain TPOXX (Tecovirimat)

- TPOXX is available from the Strategic National Stockpile through an Expanded Access Investigational New Drug (EA IND) program from CDC.
- I have procured TPOXX for 2 patients with clinical features consistent with monkeypox
  - They both had several anogenital infections when I initiated the process
  - One was confirmed positive and the other was probable with pending tests
- CDC has streamlined and simplified the process of obtaining TPOXX
  - Significantly reduced the several hours of paperwork required in the early days in May - June
  - Dr. Erica Shenoy has created a smart text tool to help you fill out the forms. Find it [here](#)
- Clinicians and care facility pharmacists can request TPOXX by contacting their state/territorial health department
  - Your local health department clinician is your friend in expediting the approval from CDC!
- You can also contact the CDC Emergency Operations Center (Phone: 770-448-7100; Email: Poxvirus@cdc.gov)
Expanded Access (EA) to Investigational Drugs for Treatment Use (EA-IND)

• An EA-IND granted by the FDA allows the use of an investigational drug
  ➢ The primary purpose must be to diagnose, monitor, or treat a serious or immediately life-threatening disease or condition
  ➢ When the disease lacks therapeutic alternatives
  ➢ Not primarily intended to obtain information about the safety or effectiveness of a drug
  ➢ Increases awareness, knowledge, and facilitates the use of experimental drugs
  ➢ While protecting patient safety and avoiding interference with the development

• EA-INDs may be provided for:
  ❑ Drug not being developed (e.g., drug target is too rare for clinical trial by sponsor)
  ❑ Drug being developed but patient(s) cannot access trial
  ❑ Drug previously approved but no longer available
  ❑ Drug has similar profile to an approved drug that is unavailable
Intermediate-Size Patient Population EA-IND

• CDC holds an intermediate-size patient population EA-IND from the FDA
  o EA for intermediate-size patient populations is for multiple patients requesting a drug for the same use
  o They are generally smaller than those typical of a treatment IND or treatment protocol
• Intermediate-size patient population EA-IND allows access to and use of TPOXX for treatment of orthopoxvirus infections, including monkeypox
• Clinicians and facilities do not need to request and obtain their own INDs.
• For facilities requiring a reliance agreement, CDC IRB will provide a pre-signed reliance agreement to sign documenting reliance on CDC IRB (huma@cdc.gov).
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<td><strong>Patient Intake Form</strong></td>
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<td><strong>FDA Form 1572</strong></td>
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<td><strong>Clinical Outcome Form</strong></td>
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</table>
Informed Consent Form

- If taking tecovirimat by mouth:
  - Patients should eat a full, fatty meal 30 minutes before tecovirimat and should take it with a full glass of water
  - The meal should be about 600 calories with 25 grams of fat (e.g., cheeseburger with fries, rice with fried chicken, pasta alfredo, bagel with cream cheese, avocado, peanut butter, ready-to-drink meal, etc.)
- Those unable to take capsules or eat a full meal (e.g., hospitalized with serious illness) may take IV tecovirimat
The most common adverse events in people who took tecovirimat were:

- Headache
- Vomiting
- Nausea
- Stomach pain
- Dizziness (only with IV tecovirimat)
- Pain/swelling/redness at the injection site (only with IV)
Low blood sugar can occur when tecaoviramt is taken with riapophine, a medicine used to treat type 2 diabetes. If you are taking riapophine, tell your healthcare provider if you get any of these symptoms of low blood sugar:

- Headache
- Hunger
- Dizziness
- Sweating
- Fast heartbeat
- Drowsiness
- Feeling jittery or shaky
- Confusion
- Weakness
- Irritability

As with any medication, there is a potential risk of an allergic reaction. An allergic reaction after receiving tecoviramt could include a rash, difficulty breathing, wheezing, sudden drop in blood pressure, causing dizziness or fainting, swelling (around the mouth, throat, or eyes), fast pulse, and sweating.

During tecoviramt treatment, a small amount of your blood (5 mL or 1 teaspoon) may be taken for tests. Possible risks of taking blood are brief pain, bleeding, bruising of the skin where the needle enters, infection at that spot, and possible infection at that spot. A trained person skilled in blood collection will collect your blood sample using a sterile technique. Please tell the doctor about any medical conditions or problems that you have.

ARE THERE RISKS RELATED TO PREGNANCY OR NURSING?
Tecoviramt has not been studied in pregnant or nursing people. It is not known if giving tecoviramt to a pregnant person would hurt the unborn child. Tecoviramt has been tested on pregnant mice and rabbits. There were no serious problems in the unborn animals. Povirvirus during pregnancy can cause serious harm to the pregnant person and unborn baby. Given that it is serious, the potential benefits of tecoviramt likely outweigh the risks. In animal studies, tecoviramt was present in animal milk. When a drug is present in animal milk it is likely to be present in human milk. Because of the potential for virus transmission through direct contact with the breastfed infant, breastfeeding is not recommended while the nursing individual has active lesions. A lactating person should consider passing breastfeeding and consider pumping and discarding breast milk during treatment.

WHAT OTHER CHOICES DO I HAVE?
There are two vaccines (Zymosan and ACAM2000), approved by the FDA, for prevention of smallpox and monkeypox disease. The vaccines can help protect people against smallpox, monkeypox or other povirus infections when given before exposure to the virus. It may also help even after exposure to virus if the vaccine is given soon after exposure (within 4 days) or may lessen the symptoms of disease when given between 4-14 days after exposure. But how well the vaccine may protect after exposure and whether the person was exposed affects how protective the vaccine is not known. The vaccines will not treat or get rid of the povirus infection or disease, if you have them. There is no proven way to treat povirus, but research is ongoing. You may benefit from supportive therapy (such as TV fluids, or medicine to control fever or pain) and antibiotics for any bacterial infections you may have. There may be other medications that your doctor may consider using to treat your infection. There may also be research studies looking at other new treatments for poviruses. You should discuss any questions you have and other choices you may have with your doctor.

WHAT ARE MY COSTS?
CDC is providing tecoviramt for free. Other costs of the hospital and medical care will not be paid by CDC. Other costs will need to be paid by your insurer, Medicare, Medicaid, or you.

WHAT IF YOU REFUSE TECOVIRAMT TREATMENT?
You have the right to refuse tecoviramt. Talk to the doctor if you do not want to get tecoviramt. Your will explain how it may affect your health and will tell you about other treatments. You also have the right to stop tecoviramt at any time without penalty especially if you have any side effects that you cannot tolerate. It will not change your regular medical care if you decide not to take it.

WHAT HAPPENS IF YOU ARE HARMED?
You will get immediate medical care if you are harmed from getting tecoviramt treatment. But CDC will not give this care. CDC does not normally pay for harm done to you because of being in a program like this. Thus, you or your insurer (such as Medicare or Medicaid) will have to pay for any care that is needed. But, you are not giving any of your rights by signing this consent form and agreeing to be treated with tecoviramt in this program.

WHAT IS THE COUNTERMEASURES INJURY COMPENSATION PROGRAM?
The Countermeasures Injury Compensation Program (CICP) is a federal program that provides compensation to certain people as a result of serious injury or death from certain medicines or vaccines, including this medicine. You can learn more about this program by visiting www.hrsa.gov/cicp or call 1-855-366-2427.

WHAT ABOUT PRIVACY?
We will keep all facts about you private to the extent allowed by applicable law. People who work for CDC, FDA, U.S. Department of Health and Human Services, and local state health authorities may look at your tecoviramt treatment and related medical records to ensure and monitor the appropriate and safe use of tecoviramt. If this information is shared with anyone else such as your name and personal information will not be used or listed. If we share photos, we will only use those that will not reveal your identity. This includes reports or any publications such as articles in scientific journals. But, CDC is allowed to give your name to public health or medical people who, for example, need to find out how you got the infection and how to prevent other cases.

WHAT IF I HAVE PROBLEMS OR QUESTIONS?
If you have questions about this treatment program or feel that you or your child have been harmed as a result of participation in this program, please contact your treating physician. If you have questions about your rights as a participant in this program, please call CDC's Human Research Protection Office at 1 (800) 584-8814 and say that you are calling about CDC protocol #404. Leave a brief message with your name and phone number. Someone will call you back as soon as possible.

WRITTEN INFORMED CONSENT FOR TREATMENT WITH TECOVIRAMT
I have read the form or it has been read to me. I have been given a chance to ask questions and my questions have been answered. I agree to (or have my child get) tecoviramt. I also agree that any samples I may give can be stored for future orthovirus-related testing.

Print Patient's Name:

Patient/Parent's Signature:

Date:

Note: If patient or parent/guardian is unable to sign, a next of kin may sign. Legally Authorized Representative Signature:

Print Name:

Date:

TRANSLATOR DOCUMENTATION (if applicable)

Translator to document if patient gave informed consent through another language other than English: I have translated this form into the language

Print Name:

Translator’s Signature:

Date:

IND 116159 for Tecoviramt (CDC #6407) Version 6.0

Informed Consent Page 4 of 5

July 20, 2023
Informed Consent Continued

- Tecovirimat and repaglinide taken together may cause severe hypoglycemia and should be avoided.
- Safety profile data in pregnancy is limited.
- The drug is free and paid by CDC.
  - Other costs will need to be paid by your insurer, Medicare, Medicaid, or you
- You have the right to refuse tecovirimat.
- The Informed Consent Form can be found [here](#).

<table>
<thead>
<tr>
<th>Document as such in the patient’s medical record and ensure the patient or patient’s legally authorized representative is made aware that tecovirimat was administered for uses for which it is not FDA-approved.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name &amp; signature of treating physician who made the determination to administer tecovirimat to patient when informed consent could not be obtained:</td>
</tr>
<tr>
<td>Name</td>
</tr>
<tr>
<td>Name &amp; signature of second physician, who is not otherwise participating in this treatment protocol, reviewing and evaluating decision to administer tecovirimat to patient:</td>
</tr>
<tr>
<td>Name</td>
</tr>
</tbody>
</table>

Notify CDC via email (regaffairs@cdc.gov) within 3 working days of tecovirimat initiation when the treatment determination was made based on the above-mentioned certification by the treating physician and an independent physician.
Patient Intake Form

• I would recommend adding the patients EMR note with pictures of the lesions if possible. CDC encourages obtaining pictures of the lesions, but it is not a must.

• Form can be found here
### Patient Intake Form Continued

**INELIGIBILITY FOR TECOVIRAMAT TREATMENT**

- [ ] Yes
- [ ] No
  - unwilling to sign informed consent
  - [ ] Yes
  - [ ] No
  - reduce tecovirimat treatment
  - [ ] Yes
  - [ ] No
  - [ ] Unknown
  - known allergy to tecovirimat and/or inactive ingredients of tecovirimat
  - [ ] Yes
  - [ ] No
  - [ ] Unknown
  - for IV tecovirimat only: patients with severe renal impairment (creatinine clearance < 30 mL/min)
  - [ ] Yes
  - [ ] No
  - [ ] NA

**MEDICAL HISTORY**

<table>
<thead>
<tr>
<th>Date of illness onset:</th>
<th>Unknown</th>
<th>Date of exposure:</th>
<th>Unknown</th>
</tr>
</thead>
</table>

- Patient started as inpatient or outpatient:
  - [ ] Inpatient, date of admission: No
  - [ ] Outpatient
- Patient was admitted to ICU:
  - [ ] Yes
  - [ ] No
- Has patient history of prior smallpox vaccinations:
  - [ ] Yes
  - [ ] No
  - [ ] Unknown
- Date(s) of vaccination:
  - [ ] Unknown
- If vaccinated with ACAM2000, was there a documented vaccine "take"?
  - [ ] Yes
  - [ ] No
- If yes, date of take: __________

**Medical History (may attach notes from medical record):**

- HIV/AIDS
  - [ ] Active
  - [ ] Historical
- Atopic dermatitis or eczema
  - [ ] Active
  - [ ] Historical
- Other skin disease:
  - [ ] Active
  - [ ] Historical
- Congenital/immune deficiency
  - [ ] Active
  - [ ] Historical
- Autoimmune/connective tissue disorder
  - [ ] Active
  - [ ] Historical
- Bone marrow/organ transplant
  - [ ] Active
  - [ ] Historical
- Leprosy
  - [ ] Active
  - [ ] Historical
- Lymphoma
  - [ ] Active
  - [ ] Historical
- Other infection(s):
  - [ ] Active
  - [ ] Historical
- Other cancer:
  - [ ] Active
  - [ ] Historical
- Other pre-existing condition(s):
  - [ ] Active
  - [ ] Historical

**Vital signs (to the extent feasible to be collected):**

<table>
<thead>
<tr>
<th>Patient Weight (kg):</th>
<th>Height (t. m.):</th>
<th>Pupil (bpm):</th>
<th>Temperature (“F”):</th>
</tr>
</thead>
</table>

### SIGNS/SYMPTOMS ON INITIAL PRESENTATION

- Number of lesions:
  - [ ] < 10 lesions
  - [ ] 10 – 100 lesions
  - [ ] > 100 lesions
- Approximate:
  - [ ] Unknown
- Size of maximal lesion (mm)
  - [ ] Unknown

**Percent of body affected (%):**

- [ ] Yes
  - Date(s): taken:
    - [ ] Unknown
  - If yes, send photos to CDC
  - [ ] No

**Clinical Narrative:** Please describe presenting illness, signs and symptoms, including type, site and circumstances of exposure, and lesion characteristics; may attach electronic summary visit from patient’s EHR.

**DISTRIBUTION OF LESIONS**

<table>
<thead>
<tr>
<th>Left</th>
<th>Right</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scalp</td>
<td>Scalp</td>
</tr>
<tr>
<td>Face</td>
<td>Face</td>
</tr>
<tr>
<td>Mouth</td>
<td>Mouth</td>
</tr>
<tr>
<td>Oral mucosa</td>
<td>Oral mucosa</td>
</tr>
<tr>
<td>Throat</td>
<td>Throat</td>
</tr>
<tr>
<td>Eye</td>
<td>Eye</td>
</tr>
<tr>
<td>Hand</td>
<td>Hand</td>
</tr>
<tr>
<td>Arm</td>
<td>Arm</td>
</tr>
<tr>
<td>Trunk</td>
<td>Trunk</td>
</tr>
<tr>
<td>Abdomen</td>
<td>Abdomen</td>
</tr>
<tr>
<td>Buttock</td>
<td>Buttock</td>
</tr>
<tr>
<td>Genitals</td>
<td>Genitals</td>
</tr>
<tr>
<td>Anus</td>
<td>Anus</td>
</tr>
<tr>
<td>Thigh</td>
<td>Thigh</td>
</tr>
<tr>
<td>Calf</td>
<td>Calf</td>
</tr>
<tr>
<td>Foot</td>
<td>Foot</td>
</tr>
</tbody>
</table>

**LIST OF MEDICATIONS**

(List all medications, especially any immunosuppressing medications and other antivirals or treatments for orthopoxvirus infection (tecovirimat can be used in conjunction with other therapies based on treating physician’s clinical judgment). Note: Co-administration of tecovirimat with tegafur may cause hypoglycemia. Monitor blood glucose and monitor for hypoglycemic symptoms during co-administration. Co-administration with midazolam may reduce concentration of midazolam; monitor effectiveness of midazolam in patients.)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage/Frequency</th>
<th>Administration route</th>
<th>Date of administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tecovirimat</td>
<td>Oral</td>
<td>IV</td>
<td>Date of first dose taken or Date prescribed</td>
</tr>
</tbody>
</table>

**OPTIONAL CLINICAL LABORATORY TESTING**

Attach a copy of clinical laboratory results (e.g., hematology, chemistry, urinalysis) if any were performed per treating physician’s clinical judgment depending on a patient’s underlying clinical conditions to monitor the safety of tecovirimat treatment as appropriate (i.e., baseline, during, post-treatment).
• Signed by one investigator per site

• The Investigator must possess the qualifications and experience to administer TPOXX

• They must abide by the protocol and agree to the FDA reporting requirements

• They should be qualified to conduct the investigation and committed to abide by regulations (https://www.fda.gov/media/78830/download)

• The form can be found here
Good to know

• Treatment with TPOXX can begin upon receipt, after informed consent is obtained
• No pre-registration is required for clinicians or facilities
• Forms requested under the EA-IND can all be returned to CDC after treatment begins.
• TPOXX use is not considered human subjects research; federal-wide assurance requirements do not apply.
• Virtual and televisits are allowed as an option for prescription of TPOXX
• If feasible, take lesion photos at baseline and post-treatment to follow lesion progression and healing

• Optional Lesion Samples for Resistance Testing

• I am planning to follow-up at 7, 14 and 21 days after starting treatment.
Tecovirimat Clinical Outcome Form

• This Form is very straightforward
• It can be found [here](#)
### ASSESSMENT OF LESIONS DURING AND AFTER TECOVIRAMIT TREATMENT

<table>
<thead>
<tr>
<th>Date of assessment</th>
<th>During Treatment</th>
<th>After Completion of Tecovirimut Course</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 1-7 (A)</td>
<td>Day 8-14 (B)</td>
</tr>
<tr>
<td></td>
<td>7-14 days after last tecovirimut dose (C)</td>
<td>Upon discharge (for patients only)</td>
</tr>
</tbody>
</table>

#### Date of assessment

- Treatment day 0
- 4 days after last tecovirimut dose

#### Approximate # of lesions

#### % of body affected

#### Size of maximal lesion (mm)

#### Any new lesions? (Yes, mark, and new lesion sampled to CDC for resistance testing, if feasible)

#### All lesions crusted and healed with new layer of skin?

#### Evidence of scarring or degeneration?

#### Structure in the genital region?

#### OPTIONAL: LESIONS/SCAB® SAMPLING FOR RESISTANCE TESTING AT CDC

Complete this section only if any samples were collected and shipped to CDC.

- Were samples collected & sent to CDC? Yes No
- Sample type
- Anatomical location of lesion
- Date of sample collection
- Date sample sent to CDC

#### OPTIONAL: PLASMA PHARMACOKINETIC (PK) SAMPLING

Complete this section only if any samples were collected and shipped to Alturas.

- Date and Time of PK Sample Collection
- Date and Time of Tecovirimut Dose
- Treatment Dose (mg/kg, IV, or PO) on PK collection

#### OPTIONAL: CLINICAL LABORATORY TESTING

Attach a copy of clinical laboratory results (e.g., hematology, chemistry, urinalysis) if any were performed per treating physician’s clinical judgment depending on the patient’s underlying clinical conditions to assess the safety of tecovirimut treatment at appropriate time points (e.g., baseline, during, post treatment).
Patients are advised to keep a diary
Additional Resources

• Dr. Erica Shenoy and her colleagues have created a smart text tool to help you fill out the forms. Find it here

• Information for Healthcare Providers on Obtaining and Using TPOXX (Tecovirimat) for Treatment of Monkeypox | Monkeypox | Poxvirus | CDC

• CFR - Code of Federal Regulations Title 21 (fda.gov)

• https://www.fda.gov/media/85675/download

• https://www.fda.gov/media/78830/download
Share your case on CURE ID

• Help the clinical community better understand the use of tecovirimat
• Submit a very brief case report form to CURE ID. It takes less than 5 minutes!
• CURE ID is a collaboration between NIH (NCATS) and FDA
• The goal is to collect and better understand real-world data on using repurposed drugs for infectious diseases.
• The collected case reports are completely de-identified and you can anonymize a submission.
• The current CURE ID case report form (disease-agnostic) can be used to share cases of use of tecovirimat, as well as any other drug treatment for monkeypox
• A monkeypox-specific case report form for both clinicians and patients is under development and is expected by the end of August.
• Visit CURE ID to register and share your treatment experience!
And Soon the TPOXX will arrive!