Treatment Guidance for Pediatric Patients with Confirmed or Suspected Mpox

Background

- Mpox is an orthopoxvirus endemic to areas of central and western Africa, which has caused a global outbreak in 2022, primarily among sexually active persons.
- Pediatric patients represented a high proportion of historical cases and deaths in Africa.
- Severe infections leading to ICU hospitalization were described in pediatric patients during the 2003 U.S. outbreak, including a 6 year old with encephalitis and a 10 year old with airway compression due to cervical lymphadenopathy and a retropharyngeal abscess.
- A small number of mild pediatric cases have been described in the 2022 outbreak.
- No pediatric deaths have been described outside of Africa (ever).
- Tecovirimat (TPOXX) inhibits the orthopoxvirus VP37 envelope wrapping protein, and is FDA-approved for treatment of smallpox and available via EA-IND for patients with Mpox.
- Tecovirimat was studied in 359 healthy adults during clinical trials, has been used to treat several hundred adults to date during the 2022 Mpox outbreak, and was used to treat a 28-month-old pediatric patient with eczema vaccinatum.

Tecovirimat (TPOXX) Indications

CDC recommends that the following pediatric patient populations be considered for treatment:

- Children and adolescents with severe disease (e.g., hemorrhagic disease, confluent lesions, encephalitis, airway obstruction due to lymphadenopathy, or other conditions requiring hospitalization)
- Children and adolescents with complications from Mpox (e.g., pneumonia, sepsis, ocular lesions, cellulitis, abscess, gastroenteritis with severe nausea/vomiting, diarrhea, or dehydration)
- Children and adolescents at high risk of severe disease:
    - Under 8 years of age*
    - Immunocompromised (e.g., human immunodeficiency virus/acquired immune deficiency syndrome infection, 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)
    - History or presence of atopic dermatitis, or 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])
    - Aberrant infections, such as those involving the eyes, face, or genitals

  *Based on limited experience, tecovirimat treatment recommendations for otherwise healthy, non-hospitalized pediatric patients <8 years of age with mild Mpox infections should be considered on a case-by-case basis after discussion of the potential risks and benefits with the parent(s)/guardian(s).

Development of Resistance to Tecovirimat

Tecovirimat has a low barrier to viral resistance. Even a single mutation in the virus, which can occur overtime as viruses replicate and spread in a population, could make the Mpox virus less susceptible to tecovirimat. It is important to use this agent judiciously while weighing this risk with the potential benefits of therapy on a case-by-case basis.

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Dosing

Table 1. Recommended Oral Dosage Instructions for 14 Days*

Weight (kg)**	Weight (lbs)	Recommended Dose (mg)*
< 6	<13	50 mg (¼ capsule) every 12 hours
6 to < 13	13 to < 28	100 mg (½ capsule) every 12 hours
13 to < 25	28 to < 55	200 mg (1 capsule) every 12 hours
25 to < 40	55 to < 88	400 mg (2 capsules) every 12 hours
40 to < 120	88 to < 264	600 mg (3 capsules) every 12 hours
120 and above	≥ 264	600 mg (3 capsules) every 8 hours

* Tecovirimat capsules should be taken within 30 minutes after a full meal containing moderate or high fat. Treatment duration is 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.

**Please refer to the following attachment for instructions on opening capsules and mixing with food for infants and children who require < 200 mg dose or who are unable to swallow capsules. Opening tecovirimat capsules and mixing with food for children weighing < 13 kg, which differs from the FDA-approved tecovirimat package insert, is allowed under this IND protocol.

Refer to Appendix I for how to order tecovirimat for patients currently admitted at SLCH.

Side Effects and Potential Risks

- The most frequently reported adverse reactions to tecovirimat are headache, nausea, abdominal pain, and vomiting.
- Co-administration with repaglinide may cause hypoglycemia. Monitor blood glucose and monitor for hypoglycemic symptoms during co-administration.
- Given the theoretical safety concern of renal toxicity related to hydroxypropyl betadex exposure, under this protocol, IV tecovirimat is contraindicated in patients with severe renal impairment (creatinine clearance clearance <30 mL/min).
- Because of the potential risk of hydroxypropyl betadex accumulation, renal function and laboratory values should be monitored during the course of therapy for all patients who receive IV tecovirimat.

References:

https://www.cdc.gov/poxvirus/monkeypox/clinicians/treatment.html
https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/fda-monkeypox-response
https://emergency.cdc.gov/coca/ppt/2022/072622_slides.pdf
Bunge EM et al. *PLOS Neg Trop Dis* 2022.
Petersen E et al. *Infect Dis Clin N Am* 2019.
Huhn GD et al. *Clin Infect Dis* 2005.
Tutu van Furth AM et al. *Euro Surveill* 2022.
Jezek Z et al. *J Infect Dis* 1987.
https://www.cdc.gov/poxvirus/monkeypox/pdf/Tecovirimat-IND-Protocol-CDC-IRB.pdf
https://www.cdc.gov/poxvirus/monkeypox/clinicians/pediatric.html

Appendix 1: Inpatient Process for Ordering Tecovirimat (TPOXX)

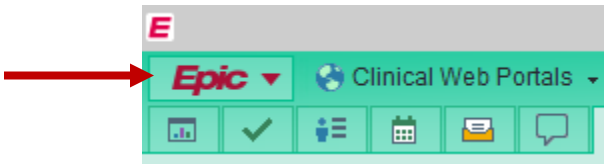
- Tecovirimat is available for inpatients who qualify for treatment
- The Infectious Diseases Consult Team must be involved
- An Infectious Diseases provider will be responsible for placing the order

A. Initial Steps

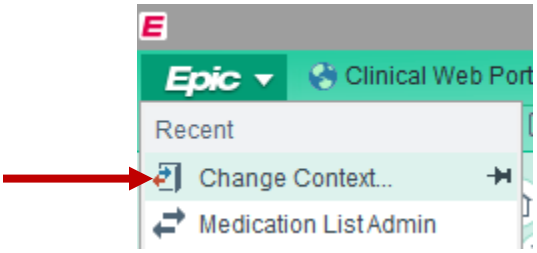
1. Contact the local health department:
   a. Contacts:
      i. Missouri: 573-751-6113
      ii. Illinois:
         1. St. Clair County DOH: 618-233-7703
         2. Madison County DOH:618-296-6200
      iii. Or CDC (Emergency Operations Center 770- 488-7100; Poxvirus@cdc.gov)
   b. Information Health Department Needs:
      a. Shipping address for tecovirimat
      b. Receiving Point-of-Contact #1 at shipping address (name, email, 24/7 monitored phone #)
      c. Receiving Point-of-Contact #2 at shipping address (name, email, 24/7 monitored phone #)
      d. Number of people to receive treatment and their weight
      e. If IV is requested, # of days (for many patients 14 vials = 7 days of IV - will be enough and then can convert to PO
      f. Days/times the shipping address location is available to receive a shipment
2. Complete Informed Consent before initiating treatment

B. Ordering Process in Epic

1. Once logged into Epic, change your clinical context by clicking on the Epic button in the far top left corner of the screen



2. In the dropdown menu, select “Change Context”



These recommendations do not establish a standard of care to be followed in every case. Each case is different and the individuals providing health care are expected to use their judgement in determining what is in the best interests of the patient based on the circumstances at the time.

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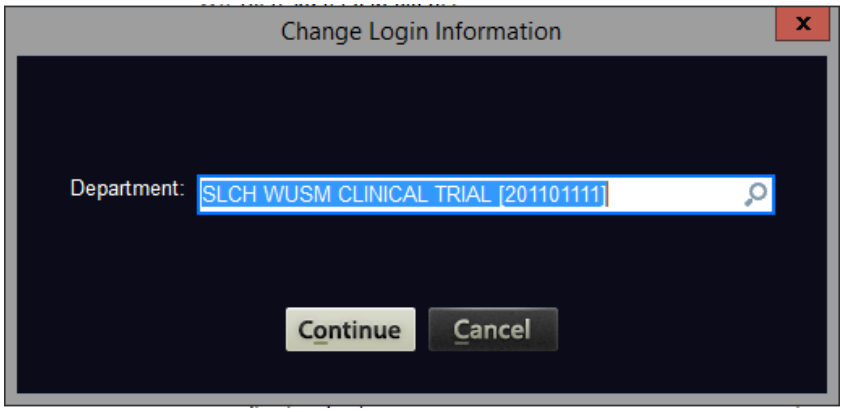
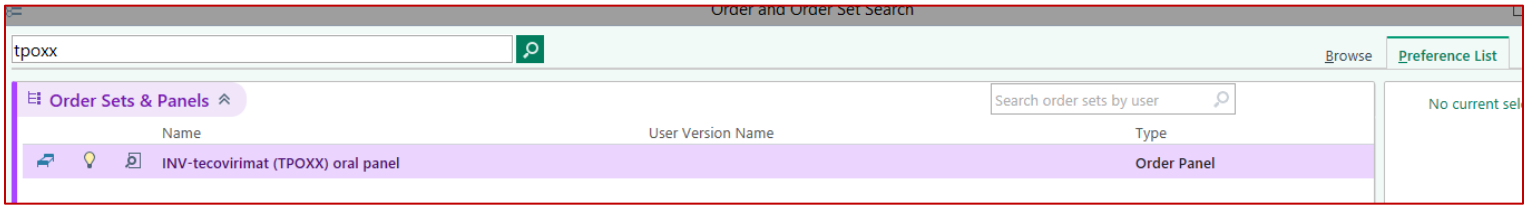
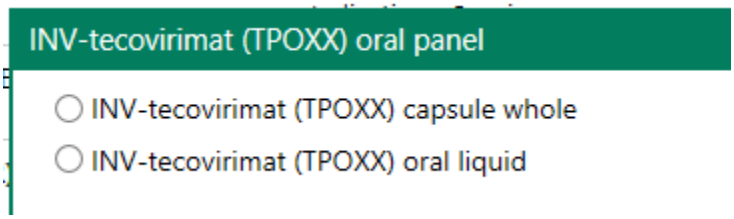
3. Type in or select the magnifying glass to set your department to SLCH WUSM CLINICAL TRIAL



4. Select CONTINUE and then open patient chart
5. In order entry, type in tecovirimat or TPOXX, and select the INV-tecovirmat (TPOXX) order panel



6. Upon entering the order panel, select either the whole capsule or oral liquid depending on patient specific factors



7. The whole capsule tecovirimat order will only populate for children who weigh at least 13 kg as whole tablets only come in a strength of 200 mg and above.
8. If intravenous tecovirimat is indicated, only pharmacy can order it through database lookup at this time. An INV intravenous order will be available soon for providers under this INV context. Contact rounding clinical specialist or inpatient pharmacy (314-454-2618) for guidance.
9. If being entered by an Infectious Diseases provider, a second-sign should not be required.
10. Upon entering the order, email SLCHIDS@bjc.org to ensure the investigational drug pharmacy team is aware.

C. Additional Forms to Submit to CDC

1. Complete required Patient Intake Form and send to CDC within 7 days of initiation of therapy
    a. Can use dot phrase ".MPXTREATMENTSTART" and send note along with form
2. If feasible, complete optional Clinical Outcome Form 3-14 days after completion of treatment
    a. Can use dot phrases ".MPXTREATMENTFINAL" and send notes along with form

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