Monkey Pox Treatment

- There are no FDA approved treatments specifically approved for monkeypox virus infections. However, monkeypox and smallpox viruses are similar (both orthopoxviruses). Thus, vaccines and medications developed against smallpox have been proposed as options via investigation use to prevent and treat monkeypox virus infections.
    - Many patients will have mild, self-limiting disease in the absence of therapy. However, some patients may benefit from anti-viral therapy (Table 1).

Table 1: Populations for Which Therapy Should be Considered

Patients with Active/Severe Disease	Patients at Risk of Severe Disease

• Confluent lesions
• Hemorrhagic disease
• Encephalitis
• Pneumonia
• Sepsis
• Other conditions requiring hospitalization
	• Lesions/infection that include implantation in eyes, mouth, or infection of the genitals or anus
	• Painful genital or anal lesions/tenesmus
	• Patients < 8 years of age
	• Pregnant or breastfeeding
	• Immunocompromised state
	  ○ Tumor necrosis factor inhibitors
	  ○ High dose corticosteroids
	  ▪ Prednisone 20mg/day (or equivalent) for ≥14 days
	  ○ Uncontrolled HIV/AIDS
	  ○ Solid organ transplant recipient
	  ○ Autoimmune disease with immunodeficiency as a clinical component
	• Generalized malignancy
	  ○ Therapy with alkylating agents
	• Leukemia
	  ○ Receipt of hematopoietic stem cell transplant < 24 months post-transplant OR ≥ 24 months w/ graft vs. host disease or disease relapse
	• Lymphoma
	• History or current atopic dermatitis
	• Active exfoliate skin conditions (burns, impetigo, VZV, HSV, severe acne, severe diaper dermatitis with extensive denuded skin, psoriasis, or keratosis follicularis
	• One or more complications
	  ○ Secondary bacterial infection
	  ○ Gastroenteritis with severe N/V/D or dehydration

Table 2: Therapeutic Options

<table>
<tr>
<td>Tecovirimat (TPOXX®, ST-246)

• Indicated for the treatment of human smallpox disease in adults and pediatrics ≥ 3kg
○ Efficacy data not available in humans.
○ Data is extrapolated from animal studies
○ Demonstrated efficacy against orthopoxviruses (includes smallpox and monkeypox)
○ Survival benefit noted when initiated within 5 days of onset however still recommended if new lesions develop past 5 days of onset
• Demonstrates ~1000 fold greater virologically activity than cidofovir
• CDC maintains a compassionate use protocol for monkeypox outbreaks available through the Strategic National Stockpile (requires IND and patient consent)</td>
<td>
<table>
<tr><th colspan="2">Dosing Adult and Pediatric - PO Dosing[α]
200 mg capsules</th></tr>
<tr><td>< 6kg</td><td>50 mg q12h [β]</td></tr>
<tr><td>6 kg to <13 kg</td><td>100 mg q12h [β]</td></tr>
<tr><td>13 kg - < 25 kg</td><td>200 mg q12h x14 days</td></tr>
<tr><td>25 to < 40 kg</td><td>400 mg q12h x14 days</td></tr>
<tr><td>40kg - < 120 kg</td><td>600 mg q12 x 14 days
(2 bottles)</td></tr>
<tr><td>≥120 kg</td><td>600 mg q8h x 14 days
(3 bottles)</td></tr>
</table>
[α] Administer within 30 minutes of moderate or high fat meal (~25g fat)
[β] Instructions on opening capsules and mixing with food

<table>
<tr><th colspan="2">Dosing Adult and Pediatric - IV Dosing[Δεζη]</th></tr>
<tr><td>3 kg to < 35 kg</td><td>6 mg/kg IV q12h up to 14 days</td></tr>
<tr><td>35 kg to < 120 kg</td><td>200 mg IV q12h up to 14 days</td></tr>
<tr><td>≥120 kg</td><td>300 mg IV q12h up to 14 days</td></tr>
</table>
[Δ]Infuse over 6 hours
[ε]Contains hydroxypropyl-β-cyclodextrin
[ζ]Use caution in: < 2 yrs; CrCl: 30-89 mL/min
[η]Store in refrigerator

• Capsules can be opened and mixed with liquid [(30mL)(i.e. Milk/chocolate milk)] or semi-solid food (i.e. applesauce/yogurt)
○ Administer within 30 minutes of preparation
○ Convert IV to PO as soon as possible
• Contraindications: CrCl < 30 mL/minute (IV formulation)
• Drug interactions: repaglinide (hypoglycemia), Midazolam (decreased. efficacy); induces CYP3A4 and inhibits CYP2C19 (not clinically relevant)
• ADRs:
○ PO: HA, nausea/vomiting, and abdominal pain, systemic reactions, cutaneous reactions
○ IV: HA and administration site reactions, systemic reaction, cutaneous reaction
• Pregnancy: no toxicity noted in mice studies
• Lactation: not recommended during active infection
○ Identified in animal milk
• Monitoring (IV): Baseline renal function and daily thereafter
</td>
</tr>
<tr>
<td>Cidofovir (Vistide®)</td>
<td>• Highly nephrotoxic agent
• Will be considered on a case by case basis if tecovirimat therapy is contraindicated</td>
</tr>
</table>

Table 3: Post-Exposure Prophylaxis (PEP)	
• JYNNEOS® ○ Live, attenuated, non-replicating Vaccinia virus ○ FDA approved for prevention of Monkeypox virus infection ○ High-risk individuals > 18 years of age exposed to Monkeypox or Smallpox ○ Use in < 18 requires a single patient EUA from the FDA ○ Provided by the WCHD via supply from CDC ○ Previous smallpox vaccination does not confer lifelong immunity to monkeypox	• Patient is eligible if ≥3 years have lapsed since receiving a smallpox vaccine • CDC recommends vaccination within 4 days from the date of exposure in order to prevent onset of the disease ○ Administration between 4–14 days after the date of exposure, may reduce symptoms of disease, but may not prevent the disease ○ Due to supply issues, the Washoe County Health Department is restricting PEP to patients presenting within 4 days of exposure • Dose: 0.5 mL subQ x2, 4 weeks apart ○ Patients are considered vaccinated 2 weeks after 2nd dose • Safe to administer in patients with eczema, exfoliative skin conditions, and HIV • Adverse reactions: Type I hypersensitivity reactions possible, Injection site reactions, fatigue, headache, and myalgias • Hypersensitivity considerations ○ Grown in primary chicken embryo fibroblast (CEF) cells ▪ Each dose contains < 500 mcg (egg) protein, ciprofloxacin (< 0.005 mcg), and gentamicin (≤0.163 mcg)
• ACAM2000® ○ Live, replicating Vaccinia virus ○ FDA EA-IND for prevention of Monkeypox ▪ Requires informed consent and other forms ○ Administered via multiple puncture technique with bifurcated needle ▪ Training videos available through the CDC	• Patient is eligible if ≥3 years have lapsed since receiving a smallpox vaccine • See JYNNEOS re: timing of vaccination from exposure • Immune response takes 4 weeks for maximal development • Following successful inoculation, a lesion (AKA a “take”) will develop and take ≥6 weeks to resolve ○ Vaccination site must remain clean and covered until it completely heals ○ Recipients must take precautions to prevent spread of vaccine virus (direct contact) during the healing period • Adverse reactions: Type I hypersensitivity reactions, pain, inflammation, erythema, fever, rash, lymphadenopathy, and complications of inadvertent inoculation • Contraindicated in the following populations: ○ Infants (< 12 months of age) ○ Congenital or acquired immunodeficiency disorders, iatrogenic immunosuppression, or those with HIV (regardless of CD4 count) ○ Eczema or other exfoliative skin conditions ○ Pregnancy ○ Cardiac disease ○ Eye disease treated with topical steroids

References:

- 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. https://www.cdc.gov/poxvirus/monkeypox/pdf/Tecovirimat-IND-Protocol-CDC-IRB.pdf. Accessed July 22, 2022.
- 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. Accessed July 21, 2022.
- Centers for Disease Control and Prevention. Interim Clinical Guidance for the Treatment of Monkeypox.cdc.gov/poxvirus/monkeypox/clinicians/treatment.html. Accessed July 21, 2022. Tecovirimat (TPOXX) [package insert]. U.S. Food and Drug Administration website. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/214518s000lbl.pdf. Revised 5.2022. Accessed July 25, 2022.
- Centers for Disease Control and Prevention. Monkeypox and Smallpox Vaccine Guidance. https://www.cdc.gov/poxvirus/monkeypox/clinicians/smallpox-vaccine.html. Accessed July 21, 2022.Centers for Disease Control and Prevention. Monkeypox Vaccine Considerations. https://www.cdc.gov/poxvirus/monkeypox/considerations-for-monkeypox-vaccination.html/ Accessed August 3, 2022.