

## Interim Guidance for Treatment of Monkeypox

### Summary

- Monkeypox is an infection caused by an orthopoxvirus. [Cases](#) are increasing rapidly. Symptoms may include fever, fatigue, lymphadenopathy, and a pimple- or blister-like rash.
- Supportive care and treatment of symptoms should be initiated for all patients with monkeypox infection. This may include medicines or other clinical interventions to control itching, nausea, vomiting, and pain.
- Antiviral treatment of monkeypox infection should be considered for people with:
  - Severe infection
  - Illness complication
  - Risk factors for progression to severe infection
- [Tecovirimat](#) (TPOXX or ST-246) is an antiviral medication available through an expanded access Investigational New Drug (EA-IND) protocol for the treatment of monkeypox infection.
- Tecovirimat is available in oral and intravenous formulations.
- For more information on prescribing or accessing tecovirimat for your patients, email [MPXtherapeutics@health.nyc.gov](mailto:MPXtherapeutics@health.nyc.gov).

### Background and Clinical Presentation Consistent with Monkeypox

Monkeypox is a disease caused by infection with an orthopoxvirus. The monkeypox virus is part of the same family of viruses as smallpox. Monkeypox symptoms are similar to smallpox symptoms but milder and can include a flu-like prodrome followed by a rash. Prodromal symptoms might not develop or can occur concurrently with or after rash onset, and may include fever, headache, muscle aches, swollen lymph nodes, and fatigue. Patients may not experience the entire constellation of these symptoms.

The rash often starts in a mucosal area, including the mouth, anogenital or rectal areas, and may remain in a limited area or become more widespread to the face, torso, or extremities (including palms or soles). The initial rash has also been documented in other non-mucosal locations. Lesions may start as a macule and then progress to papule, vesicle, pustule, and then scab (see photo examples at [Centers for Disease Control and Prevention \(CDC\) Monkeypox Clinical Recognition webpage](#)).

Pain and pruritus may be prominent and disproportionate to rash appearance. Severe proctitis has been a presenting symptom and can be associated with tenesmus and rectal bleeding. Pain

may be severe enough to interfere with basic functions such as eating, urination, and defecation and can cause significant patient distress.

Co-infections with sexually transmitted infections, group A strep pharyngitis, and other viruses (e.g., varicella zoster virus or VZV) have been reported. It is important to evaluate for and treat other potential infections as appropriate.

### **Supportive Care**

Supportive care includes maintenance of adequate fluid balance, pain management, treatment of bacterial superinfections of skin lesions and treatment of co-occurring sexually transmitted or superimposed bacterial skin infections. Providers should address these symptoms adequately and early to prevent hospitalizations.

Skin lesions should be kept clean and dry when not showering or bathing to prevent bacterial superinfection. Pruritus can be managed with oral antihistamines and inert, anti-irritant topical agents such as calamine lotion or petroleum jelly.

For oral lesions, compounds such [“magic” or “miracle” mouthwashes](#) (prescription solutions used to treat mucositis) can be used to manage pain. Oral antiseptics can be used to keep lesions clean (e.g., chlorhexidine mouthwash). Topical benzocaine/lidocaine gels can be used for temporary relief, especially to facilitate eating and drinking, but should be limited to recommended doses.

For painful genital and anorectal lesions, warm [sitz baths](#) lasting at least 10 minutes several times per day may be helpful. Topical benzocaine/lidocaine gels or creams at the recommended doses may also provide temporary relief.

Proctitis can occur with or without internal lesions and, though often manageable with appropriate supportive care, can progress to become severe and debilitating. Stool softeners such as docusate should be initiated early. Sitz baths, as described above, are also useful for proctitis, and may calm inflammation. Similarly, over the counter pain medications such as acetaminophen can be used. Pain from monkeypox proctitis may require prescription medications, use of which should be balanced with the possibility of side effects, like constipation. Proctitis may additionally be accompanied by rectal bleeding. Though rectal bleeding has been observed to be self-limited, patients with rectal bleeding should be evaluated by a healthcare provider.

Nausea and vomiting may be controlled with anti-emetics as appropriate. Diarrhea should be managed with appropriate hydration and electrolyte replacement. The use of anti-motility agents is not generally recommended given the potential for ileus.

## Antiviral Treatment: Tecovirimat

Tecovirimat (TPOXX or ST-246) is an antiviral medication that is [FDA-approved to treat smallpox](#). In animal studies, tecovirimat has been shown to decrease the chance of dying from infections with orthopoxviruses when given early in the disease course. In people, efficacy studies have been limited to drug levels in blood and a few case studies. In a case series of people with monkeypox infection, one patient received tecovirimat with results suggesting tecovirimat might shorten duration of illness and viral shedding, though efficacy is unknown ([Adler, 2022](#)).

Tecovirimat is not yet approved for treatment of monkeypox in the United States, though it has been [approved for monkeypox treatment in Europe](#). As such, tecovirimat can only be released by the Centers for Disease Control and Prevention (CDC), which holds a non-research, [expanded access Investigational New Drug \(EA-IND\) protocol](#) for use of tecovirimat as treatment of confirmed or presumed monkeypox infection. Informed consent is required for all patients treated with tecovirimat.

### *Considerations for Use of Tecovirimat*

Tecovirimat should be considered broadly for treatment of monkeypox, and patient selection is at the discretion of the treating clinician under the EA-IND. Both oral and intravenous formulations are available. Empiric treatment can be considered if there is appropriate clinical indication prior to laboratory confirmation, especially in the context of limited or delayed testing.

Situations where tecovirimat should be prioritized for use include:

- Patients with severe disease, defined by evidence of sepsis or other clinical evidence of viremia, and lesion location or type<sup>a</sup>
- Patients with evidence of illness complications<sup>b</sup> or patient hospitalization
- Patients at high risk for severe disease, defined as patients with severe immunocompromising conditions;<sup>c</sup> patients less than 8 years of age; patients who are pregnant or breastfeeding; patients with diseases that could increase risk of stricture or fistula such as inflammatory bowel disease; and patients with significant active exfoliative dermatologic conditions.<sup>d</sup>

<sup>a</sup> Lesion location or type: Confluent lesions, lesions in anatomical areas at special risk of scarring or stricture, such as those near or directly involving the eye, mouth, rectum, or urethra.

<sup>b</sup> Complications: Severe or difficult to control secondary bacterial infection (including sepsis), proctitis (particularly with tenesmus, challenges in pain control, or rectal bleeding), gastroenteritis with nausea/vomiting, bronchopneumonia, and encephalitis.

<sup>c</sup> Severe immunocompromising conditions include people living with HIV who are not virally suppressed or have active opportunistic infection; hematologic malignancy; history of solid organ transplantation; hematopoietic stem cell transplant <24 months post-transplant or ≥24

months but with graft-versus-host disease or malignant disease relapse; any condition actively requiring chemotherapy, radiation, or continuous or high-dose systemic corticosteroids; and autoimmune disease requiring immunosuppression or with immunodeficiency as a clinical component.

<sup>d</sup> Significant dermatologic conditions include presence of atopic dermatitis or other active exfoliative skin conditions or infections (e.g., psoriasis, Darier disease [keratosis follicularis], eczema, impetigo, primary varicella, zoster, or herpes).

### *Absorption Considerations and Adverse Effects of Tecovirimat*

**Oral tecovirimat:** Drug absorption of the oral formulation is dependent on adequate, concurrent intake of a full, fatty meal. Standard adult oral dosing of tecovirimat is 600mg every 12 hours for 14 days. For most adults, this will require taking 3 pills every 12 hours. Therefore, ability to tolerate oral intake of a full meal twice a day is required. Reported adverse effects include headache (12%), nausea (5%), abdominal pain (2%), and vomiting (2%). Neutropenia was found in one study participant.

**IV tecovirimat:** 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 patients younger than 2 years of age given immature renal tubular function. Reported adverse effects of the IV formulation include infusion site pain (73%), infusion site swelling (39%), infusion site erythema (23%), infusion site extravasation (19%), and headache (15%).

### *Who Should not Receive Tecovirimat*

People who are ineligible for tecovirimat treatment under EA-IND include those unwilling to sign informed consent documentation or those with a known allergy to the drug or its components.

### *Requesting Tecovirimat*

Tecovirimat is only available through the federal Strategic National Stockpile. For facilities interested in prescribing tecovirimat for eligible patients under the EA-IND, medication must be requested through the NYC Department of Health and Mental Hygiene. NYC has also partnered with a local pharmacy to provide delivery of the medication to NYC residents at their preferred address. For more information on prescribing or accessing tecovirimat for your patients, email [MPXtherapeutics@health.nyc.gov](mailto:MPXtherapeutics@health.nyc.gov). Do not send patient identifiers to this email address.

### **Other Therapeutic Agents**

Other therapeutic options are under investigation and include the antivirals cidofovir and brincidofovir, as well as Vaccinia Immune Globulin Intravenous (VIGIV). The use of cidofovir has

been limited by serious renal toxicity. To date, use of VIGIV has no proven benefit in the treatment of monkeypox and it is unknown whether a person with severe monkeypox infection will benefit from treatment with VIGIV. More information and updates on the status of these therapeutics in monkeypox treatment can be found on the [CDC Monkeypox Treatment Information for Healthcare Professionals webpage](#).

## References

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The NYC Health Department may change recommendations as the situation evolves.

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