

Interim Guidance for Treatment of Monkeypox

Summary

- **Monkeypox 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 pain, itching, nausea and vomiting.
- Antiviral treatment of monkeypox infection should be considered for people with severe illness, illness complications or risk factors for severe disease.
- **Tecovirimat** (TPOXX or ST-246) is an antiviral medication available through the Centers for Disease Control and Prevention (CDC) that is being used to treat monkeypox infection under the **expanded access investigational new drug protocol (EA-IND)**.
- Tecovirimat should be prescribed when indicated for patients who have a positive test result, or are awaiting test results and have a clinically compatible illness.
- Any health care facility or provider can prescribe tecovirimat if they can adhere to the EA-IND protocol. Tecovirimat can be prescribed upon obtaining **informed consent** from the patient. Additional forms can be submitted to the CDC after initiating treatment.
- All patient visits can be done via telemedicine.
- Providers in NYC who want to prescribe tecovirimat for their patients and can adhere to the EA-IND protocol can email **MPXtherapeutics@health.nyc.gov** for information on the home delivery service using supplies from the NYC pharmacy or to request supplies for an on-site pharmacy at their facility.

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 nonmucosal locations. Lesions may start as a macule and then progress to papule, vesicle, pustule and then scab. Visit [cdc.gov/monkeypox](https://www.cdc.gov/monkeypox) and search for **Clinical Recognition** to see examples of monkeypox rash photos.

Pain and pruritus (itching) may be prominent and disproportionate to rash appearance. Oral mucositis is well known with monkeypox, but in the current outbreak, severe proctitis (inflammation of the lining of the rectum and lower digestive system) has been a presenting symptom and can be associated with rectal tenesmus (cramping) and bleeding. Penile lesions, especially around the foreskin, can cause severe pain and swelling and lead to complications such as phimosis or paraphimosis. Dysuria or hematuria may also occur due to lesions in and around the urethra. Pain may be severe enough to interfere with basic functions such as eating, urination and defecation, and can cause significant distress.

Coinfections with sexually transmitted infections, including gonorrhea, chlamydia and syphilis; group A strep pharyngitis; superimposed bacterial infections of lesions; and other viruses (for example, varicella zoster virus or herpes simplex virus) have been reported. It is important to evaluate for and treat other potential infections as appropriate.

Monkeypox occurring in **people living with HIV** or other immunocompromising conditions, who are **pregnant or breastfeeding**, or who have a history of eczema or certain other skin conditions may be at increased risk for severe disease. This makes it especially important to monitor symptoms and offer antiviral treatment early in the disease course.

Supportive Care

Supportive care includes maintenance of adequate fluid balance, pain management, treatment of bacterial superinfections or co-occurring sexually transmitted or superimposed bacterial skin infections. Providers should give anticipatory guidance and 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) and cooling lotions (such as menthol or camphor lotions). Warm oatmeal baths can also reduce itching and pain. Instruct patients to seek care if they observe increases in pain, redness, swelling, or milk or cloudy fluid at the site of the sores.

For oral lesions, patients can rinse their mouths with salt water at least four times per day. Alcohol-free oral antiseptics (such as Listerine Zero Alcohol and chlorhexidine mouthwash) can be used to keep lesions clean. For pain, patients can suck on ice chips or ice pops, or use compounds such as **“magic” or “miracle” mouthwashes** (prescription solutions used to treat mucositis). Topical treatments such as patches (for example, Dentemp Canker Covers) and benzocaine or 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 or lidocaine gels or creams at the recommended doses may provide temporary relief. Instruct patients to seek care if they have

blood in their urine, difficulty urinating, are unable to retract their foreskin (phimosis), or their foreskin cannot return to its normal position after being retracted (paraphimosis).

Proctitis can occur with or without internal or external 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. Over-the-counter pain medications (such as acetaminophen and ibuprofen) can be used (including together, alternating, if needed). Topical anesthetics such as dibucaine ointment, often used for hemorrhoids, and lidocaine gel have been effective for temporary relief. Pain from monkeypox proctitis may require prescription medications (such as gabapentin or opioids), the 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 should be evaluated by a health care provider.

For gastrointestinal symptoms, 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 (inability of the intestine to contract normally).

Antiviral Treatment: Tecovirimat

Tecovirimat 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 the duration of illness and viral shedding, though the efficacy is unknown.¹

Tecovirimat is not yet approved for treatment of monkeypox in the U.S., though it has been **authorized for monkeypox treatment in Europe**. Therefore, tecovirimat is only available through the federal strategic national stockpile (SNS) and must be prescribed under a CDC-held, non-research, EA-IND protocol for the use of tecovirimat as treatment of adults and children with confirmed or presumed monkeypox infection.

Considerations for Use of Tecovirimat

Tecovirimat should be considered for any patient with diagnosed or suspected monkeypox in whom the drug is not absolutely contraindicated and meets the criteria in the following table. Patient selection is at the discretion of the treating clinician under the EA-IND. Both oral and intravenous formulations are available. Any patient with suspected monkeypox should be

¹Adler H, Gould S, Hine P, et al. Clinical features and management of human monkeypox: a retrospective observational study in the UK. *The Lancet*. 2022; 22(8):1153-1162. doi: [10.1016/S1473-3099\(22\)00228-6](https://doi.org/10.1016/S1473-3099(22)00228-6)

tested; however, 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:

Indication	Notes
Patients with severe disease, defined by evidence of sepsis or other clinical evidence of viremia, and lesion location or type	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.
Patients with evidence of illness complications or patient hospitalization	Complications: severe or difficult to control secondary bacterial infection (including sepsis), proctitis (particularly with tenesmus, challenges in pain control or rectal bleeding), urethritis, phimosis, gastroenteritis with nausea or vomiting, bronchopneumonia, and encephalitis.
Patients at high risk for severe disease, defined as patients with severe immunocompromising conditions; patients younger than age 8; 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	<p>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 less than 24 months post-transplant or greater than or equal to 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.</p> <p>Significant dermatologic conditions include presence of atopic dermatitis or other active exfoliative skin conditions or infections (for example, psoriasis, Darier disease [keratosis follicularis], eczema, impetigo, primary varicella, zoster or herpes).</p>

How To Prescribe and Access Tecovirimat

Any health care facility or provider, or system can prescribe tecovirimat under the CDC's EA-IND protocol. The EA-IND was recently simplified to make it easier for providers to prescribe tecovirimat to patients, including to allow the use of telemedicine for all patient encounters (initial and follow-up visits) if the patient can submit the signed consent form electronically.

The decision to prescribe tecovirimat is based on clinical judgement and discussions between the clinician and patient. Facilities and providers should take the necessary steps to make sure they are able to prescribe tecovirimat (in compliance with the EA-IND's requirements) when indicated to ensure timely treatment for patients. Tecovirimat is provided at no cost by the federal government. Providers can prescribe for individual patients as needed from a dedicated NYC supply managed by a partner pharmacy. In planning for future tecovirimat use, providers can also coordinate with the NYC Department of Health and Mental Hygiene (NYC Health Department) to request a supply from the SNS to have on-site at a facility or health system pharmacy.

Follow these steps to prescribe tecovirimat for eligible patients:

1. Have the patient sign the **Informed Consent Form**.
2. Email **MPXtherapeutics@health.nyc.org** to receive instructions on how to:
 - Record patient identifiers and indication for treatment in a Health Insurance Portability and Accountability Act-compliant, secure, web-based REDCap form
 - Arrange to have individual prescriptions delivered to your site or directly to the patient by the NYC pharmacy courier service
3. Submit the following to the CDC:
 - **U.S. Food and Drug Administration Enrollment Form 1572**
 - This is a facility and provider enrollment form, and is not required for each patient. Only one form is required for each facility or provider. The form, once submitted, will cover all prescriptions for that provider or providers within a facility. Facilities and providers can enroll at any time and submit this form in advance of prescribing tecovirimat to patients.
 - If submitting for the first time to prescribe tecovirimat for a patient, it should be **submitted** within three days of starting treatment for the patient.
 - The two EA-IND forms (the **Patient Intake Form** and signed and completed **Informed Consent Form**) required for each individual prescription. These forms can be submitted after treatment begins, but ideally within three days of starting treatment for each patient.
4. Conduct two follow-up visits – one while the patient is on treatment (ideally between days 7 and 14) and another after treatment is completed. Afterward, submit the required **Clinical Outcome Form** to the CDC.
5. Report life-threatening or serious adverse events associated with tecovirimat by sending a completed **MedWatch Form** to **regaffairs@cdc.gov** within 72 hours of awareness.

Facilities or providers interested in ordering a supply of tecovirimat to maintain at an on-site pharmacy or serving as a referral site that is set up to prescribe tecovirimat for patients who do not have a primary care provider can email MPXtherapeutics@health.nyc.org.

Technical Assistance

Facilities or providers interested in ordering a supply of tecovirimat to maintain at an on-site pharmacy, requesting instruction and assistance with the EA-IND paperwork (or other institutional approvals or review board issues), or serving as a referral site that is set up to prescribe tecovirimat for patients who do not have a primary care provider can email MPXtherapeutics@health.nyc.org for technical assistance. Providers who are unable to complete the required EA-IND forms to prescribe tecovirimat can also reach out to MPXtherapeutics@health.nyc.org for help referring patients to another provider. However, at this time, there are prolonged wait times with an insufficient number of providers who are able to accept external referrals. Capacity is also limited. **Do not send patient identifiers to this email address.**

For more information on the EA-IND protocol and associated forms, visit [cdc.gov/monkeypox](https://www.cdc.gov/monkeypox) and search for **Obtaining and Using TPOXX (Tecovirimat)**.

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 (ideally about 600 calories and 25 grams of fat). Standard adult oral dosing of tecovirimat is 600 milligrams (mg) every 12 hours for 14 days. For most adults, this will require taking three 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 less than 30 mL/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 age 2 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%).

Drug-drug interactions: Significant interactions have been reported in healthy adults with co-administration of repaglinide (hypoglycemia) and midazolam (decreased effectiveness of midazolam). According to recent **CDC guidance** and the **University of Liverpool**, clinically relevant drug interactions that may require dose adjustment would be anticipated only between tecovirimat and the non-nucleoside reverse transcriptase inhibitors (NNRTIs) doravirine and rilpivirine as well as the CCR5 antagonist maraviroc. Dose increases for

doravirine, rilpivirine and maraviroc should be considered when co-administered with tecovirimat and for two weeks after completion of tecovirimat therapy. When co-administering tecovirimat with long-acting cabotegravir or rilpivirine, consider adding oral rilpivirine 25 mg once daily during treatment with tecovirimat and for approximately two weeks after treatment (as any reduction in rilpivirine exposure may persist for up to 14 days after stopping tecovirimat). Alternatively, if unable to obtain oral rilpivirine, consider adding the oral ART regimen the patient was taking prior to initiation of long-acting cabotegravir or rilpivirine. Continue that oral regimen for two weeks after completing tecovirimat.

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 New York City Department of Health and Mental Hygiene (NYC Health Department). 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. Do not send patient identifiers to this email address.

Racism as a Public Health Crisis and Treatment Decisions

The NYC Board of Health **has resolved that racism is a public health crisis** and committed to shifting resources and power to the communities that bear the greatest burden of marginalization racism, and health inequities. The current monkeypox outbreak will disproportionately impact people of color and people experiencing housing instability or poverty. Potential delays in testing and treatment for people of color will emerge without concerted efforts to address barriers owing to the compounding effects of racism. Providers should take the impacts of limited access to information, resources and services for these communities into account in operational, institutional and treatment decisions.

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. Brincidofovir is not currently available through the SNS.

Visit [cdc.gov/poxvirus/monkeypox/clinicians/treatment.html](https://www.cdc.gov/poxvirus/monkeypox/clinicians/treatment.html) for information and updates on the status of these therapeutics in monkeypox treatment.

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

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