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HUMAN SERVICES

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ROY COOPER • Governor KODY H. KINSLEY • Secretary MARK BENTON • Deputy Secretary for Health SUSAN KANSAGRA • Assistant Secretary for Public Health Division of Public Health

Interim Guidance for NC Healthcare Providers Tecovirimat in Treatment of Mpox*

* NC DHHS materials will use "mpox" (formerly monkeypox) going forward to address concerns and stigma associated with prior terminology. This change also aligns with the recent decisions of the CDC and World Health Organization.

*Note that this information will be updated as the situation evolves or processes change

Purpose: To provide situational awareness for the current Mpox outbreak, as well as guidance for use of Tecovirimat in treatment of persons presumed to have or diagnosed with Mpox virus. Providers should be aware that Tecovirimat is available under an Expanded Access Investigational New Drug protocol, which involves request of the medication from NC Department of Health and Human Services (NC DHHS) and attendant enrollment process, as well as completion of federal regulatory paperwork (see Appendix B). Informed consent must be signed prior to initiation of therapy; other paperwork may be completed within 3 days.

Summary

- On April 28, 2023, the tecovirimat request process was updated. Providers and facilities interested in prescribing tecovirimat for eligible patients under the EA- IND must request it through federal request agencies:
 - Providers wishing to request oral tecovirimat will need to refer patients to a clinical research site found at <u>STOMP (stomptpoxx.org)</u> or contact the call center at 1-855-876-9997.
 - Providers wishing to order IV tecovirimat should contact <u>phpr.nc@dhhs.nc.gov</u>, or contact the NC PHP&R on-call line at 1-888-820-0520.
- Mpox is an infection caused by an orthopoxvirus. <u>Cases</u>, while declining, continue to be reported globally, nationally, and in North Carolina. While rare, deaths have also occurred in the US. Anyone can get mpox, but many of the cases identified in the current outbreak have been in men who have sex with men.
- Symptoms may include fever, fatigue, lymphadenopathy, and a pimple- or blister- like rash. MPXV infection is often mild and self-limiting in the absence of specific therapy. However, the prognosis depends on multiple factors, such as previous vaccination status, initial health status, concurrent illnesses, and comorbidities. Some patients have experienced severe, debilitating pain and pruritis; as well as co-infection with STIs, making it important to evaluate need for treatment.
 - Supportive care and treatment of symptoms should be initiated for all patients with mpox infection. This may include medicines or other clinical interventions to control itching, nausea, vomiting, and pain. See <u>Interim Clinical Guidance for the Treatment of Mpox | CDC</u>.



- Antiviral treatment of mpox infection should be considered for people with:
 - Severe infection

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- o Illness complication
- Risk factors for progression to severe infection (e.g., pregnancy or HIV)
- o Painful lesions of mouth, anogenital or other sensitive anatomical areas
- Ocular involvement
- Provider's clinical determination of need
- <u>Tecovirimat</u> (TPOXX or ST-246) is an antiviral medication available in oral and IV formulations through an expanded access Investigational New Drug (EA-IND) protocol for the treatment of mpox infection in children and adults.
- On September 15, 2022, CDC and FDA updated <u>guidance to limit broad use</u> of TPOXX, due to concerns of drug resistance. Providers are asked to use discretion and follow clinical guidelines when considering prescribing TPOXX.
- On November 17, 2022, CDC released an <u>health update</u> informing health officials of two documented cases of drug resistance to TPOXX in patients with severe disseminated disease, requiring inpatient treatment and prolonged use of TPOXX. The health update also provided information on the availability of brincidofovir from SNS via <u>FDA request</u>, and clinical considerations for use in patients.
- On March 3, 2023 CDC released <u>Interim Clinical Treatment Considerations for Severe</u> <u>Manifestations of Mpox</u>. These treatment considerations for severe cases represent the most currently available clinical and animal data available on all medical countermeasures being used to treat mpox, until data from clinical trials become available. Treatment options available from the Strategic National Stockpile are listed in Appendix A.

Requesting Tecovirimat

- Providers wishing to request oral Tecovirimat will need to refer patients to a clinical research site found at <u>STOMP (stomptpoxx.org)</u> or call contact the call center at 1-855-876-9997.
- For ordering of IV Tecovirimat contact <u>phpr.nc@dhhs.nc.gov</u>, or contact the NC PHP&R on-call line at 1-888-820-0520. A transfer of available, in-state products will be sought first. If a transfer is not possible, PHPR will facilitate a request to CDC.
- Providers in need of additional medical countermeasure assistance can contact NC PHP&R at phpr.nc@dhhs.nc.gov or 1-888-820-0520.

Reporting Inventory and Administration of Tecovirimat

- Administrations of tecovirimat may be updated daily <u>but must be reported by 5 PM every</u> <u>Tuesday in the Healthcare Provider Ordering Portal (HPOP)</u>. This is a requirement of ASPR/SNS.
- Inventory should be reported as bottles on hand.
- Administrations should be reported as courses provided.



• See the <u>Appendix C. Healthcare Provider Ordering Portal (HPOP) Inventory Reporting Guide for</u> <u>detailed information regarding inventory and administration.</u>

Handling Expired or Soon to Expire Products

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The latest expiration date information for mpox vaccines and treatment supplied by the Strategic National Stockpile can be found on <u>ASPR's MPOX SNS webpage (aspr.hhs.gov/SNS/pages/Mpox.aspx)</u>.

- Currently, no extension of expiration dates for oral tecovirimat or Jynneos is anticipated. Providers with expired products should follow their own drug disposal protocols. It is requested that providers maintain records of lot numbers and quantities of products that are destroyed. Disposal information should also be reported in <u>HPOP</u>.
- IV tecovirimat <u>may</u> be eligible for expiration extensions in the future. **Providers are strongly** encouraged to continue storing IV tecovirimat even beyond current expiration dates. As more information becomes available, expiration dates will be updated on the ASPR MPOX SNS webpage mentioned above.
- ASPR is not currently replacing courses of expired IV tecovirimat. Providers in need of IV tecovirimat for patient care can request product following the procedure outlined in the "Requesting Tecovirimat" section above.

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Mpox is a disease caused by infection with an orthopoxvirus. The mpox virus is part of the same family of viruses as smallpox. Mpox symptoms are like 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 <u>Centers for Disease</u> <u>Control and Prevention (CDC) Mpox Clinical Recognition webpage</u>).

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.



Testing and Reporting

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Information on sample collection, transport, testing and reporting to local public health can be found in this NC DHHS <u>provider memo.</u>

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 <u>"magic" or "miracle" mouthwashes</u> (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 <u>sitz baths</u> 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 mpox 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 orthopox viruses 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 mpox infection, one patient received tecovirimat with results suggesting tecovirimat might shorten duration of illness and viral shedding, though efficacy is unknown (<u>Adler, 2022</u>).

In the United States, Tecovirimat is not FDA approved for treatment orthopox infection. However, it is available through the Centers for Disease Control and Prevention (CDC) under a non-research, <u>expanded</u> <u>access Investigational New Drug (EA-IND) protocol that allows for the use of tecovirimat for primary or early empiric treatment of non-variola orthopoxvirus infections, including mpox, in adults and children of all ages. Informed consent is required for all patients treated with tecovirimat.</u>

Considerations for Use of Tecovirimat

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Tecovirimat should be considered for treatment of mpox on a case by case basis, and patient selection is at the discretion of the treating clinician under the EA-IND. Both Oral and intravenous formulations of TPOXX are available. Use of intravenous TPOXX should be reserved for patients who cannot swallow oral medications. Patients receiving intravenous TPOXX should be switched to oral TPOXX as soon as they are capable of swallowing oral medications. These patients also need to be able to consume a fatty meal with medication. Instructions for opening and mixing TPOXX capsules with food can be found <u>here</u>."

Empiric treatment should only be considered if there is appropriate clinical indication prior to laboratory confirmation, especially in the context of limited or delayed testing. Use of tecovirimat does not factor into isolation timeframe.

- Assessment for use can be managed either in person or via telehealth visit.
- Informed consent must be signed prior to initiation of therapy; other paperwork may be completed within 3 days. Electronic signature is acceptable.
- Prescribing physicians can provide TPOXX under CDC's IRB approval (institutional IRB review is not necessary).
- On September 15, 2022, CDC and FDA updated <u>guidance to limit broad use</u>, due to concerns of drug resistance. <u>Recent interim data</u> from pre-clinical trials and a patient case study indicates that the VP37 protein, universal to all orthopox viruses, can mutate and reduce TPOXX antiviral activity. Providers are asked to consider the following before prescribing TPOXX:
 - \circ $\;$ Lack of efficacy data for use of TPOXX in people with infection
 - \circ $\;$ Lack of data indicating which patients would benefit most from use of TPOXX $\;$
 - Concern for resistance and reducing drug efficacy
 - Use is considered for those meeting clinical criteria
- CDC and FDA are encouraging providers to enroll patients, when possible, in the <u>NIH clinical trial</u> assessing the safety, efficacy, and resistance profile of TPOXX. Patients unable to enroll in the clinical trial still need to follow CDC's expanded access IND protocol.

Situations where tecovirimat should be prioritized for use include:



- People with mpox virus aberrant infections that include accidental implantation in eyes, mouth, or other anatomical areas where mpox virus infection might constitute a special hazard (e.g., the genitals or anus)
- Patients with severe disease, defined by evidence of sepsis or other clinical evidence of viremia, and lesion location or type^a
- Patients with evidence of illness complications^b or patient hospitalization
- Patients at high risk for severe disease, defined as patients with severe immunocompromising conditions^c; 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.
- Provider's clinical determination of need

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Check CDC's Interim Clinical Guidance for the Treatment of Mpox for the most up to date treatment considerations.

^a 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.

^b 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.

^c 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 \geq 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.

^d 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).

Contraindications

- Persons unwilling to sign informed consent documentation for treatment under EA-IND are ineligible.
- Those with a known allergy to the drug or its components.

Precautions

- Significant interactions have been reported in healthy adults with co-administration of repaglinide (hypoglycemia) and midazolam (decreased effectiveness of midazolam).
- Monitoring of renal function is recommended in pediatric patients < 2 years of age
- IV formulation should not be administered to patients with severe renal impairment (CrCl <30mL/min).



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%).

Extended Use Considerations

Patients who are severely immunocompromised may require extended use of therapies to • eliminate the mpox virus. Extended use of TPOXX past 14 days can be considered on a dayto-day basis, and/or the concomitant use of multiple therapies can also be considered (see Other Therapeutic Agents section below.)

Reports of Resistance

- Rare, isolated cases of laboratory-confirmed tecovirimat resistance have been reported in • patients with immunocompromising conditions and progressive, severe manifestations of mpox who had received prolonged courses (>14 days) of tecovirimat.
- A CDC Health Advisory issued November 17, 2022, contains guidance for identification of • resistance in patients who, after completing 14 days of tecovirimat treatment, experience persistent or newly emergent mpox lesions.
- No cases of transmission of tecovirimat-resistant virus have been documented.
- CDC and FDA are encouraging providers to enroll patients, when possible, in the NIH clinical trial (STOMP Trial) assessing the safety, efficacy, and resistance profile of TPOXX.



Other Therapeutic Agents

Other therapeutic options are under investigation and include the antivirals cidofovir and <u>brincidofovir</u>, as well as Vaccinia Immune Globulin Intravenous (VIGIV). Patients who have or are at risk of severe disease progression (patients with HIV and CD4 counts<350 mm³, severely immunocompromised, etc.) may be eligible for use of multiple concurrent therapies, depending on individual clinical consideration. Communication with infectious disease specialists or public health officials, along with the CDC, is encouraged prior to initiating multiple therapies.

<u>Brincidofovir</u>- prodrug of cidofovir available from the SNS that is FDA approved for treatment of smallpox in adults, pediatrics, and neonates. Providers will need to contact the FDA directly to submit a <u>single patient</u> <u>emergency use investigational new drug (e-IND) request</u>. Brincidofovir can be considered for treatment of mpox based on the following clinical criteria:

- Positive mpox test result
- Currently have severe disease or risk of progression to severe disease
- Either of the following:
 - experienced significant disease progression while taking tecovirimat, or initial improvement followed by worsening of symptoms (recrudescence) while taking tecovirimat
 - o ineligible or have a contraindication to tecovirimat

<u>Cidofovir</u>- can be obtained through CDC's SNS, but it's use has been limited by serious renal toxicity. <u>VIGIV</u>- has no proven benefit in the treatment of mpox and it is not known if a person with severe mpox infection will benefit from VIGIV. VIGIV is not prepositioned by the USG. It is available upon clinician request to CDC on a case-by-case basis. To request VIGIV, clinicians can contact the CDC Clinical Consultation Team by email (<u>poxvirus@cdc.gov</u>) during business hours, or for urgent clinical situations, contact the CDC Emergency Operations Center (770-488-7100).

More information and updates on the status of these therapeutics in mpox treatment can be found on the <u>CDC Mpox Treatment Information for Healthcare Professionals webpage</u>.

References

- Adler H, Gould S, Hine P, Snell LB, Wong W, Houlihan CF, Osborne JC, Rampling T, Beadsworth MB, Duncan CJ, Dunning J. Clinical features and management of human mpox: a retrospective observational study in the UK. *The Lancet Infectious Diseases*. 2022 May 24. <u>https://doi.org/10.1016/S1473-3099(22)00228-6</u>
- CDC. Guidance for Tecovirimat Use Under Expanded Access Investigational New Drug Protocol during 2022 U.S. Mpox Cases. Updated September 15, 2022. <u>https://www.cdc.gov/poxvirus/mpox/clinicians/Tecovirimat.html</u>
- European Medicines Agency. Tecovirimat. https://www.ema.europa.eu/en/medicines/human/EPAR/tecovirimat-siga
- Food and Drug Administration. Tecovirimat package insert. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/214518s000lbl.pdf
- Food and Drug Administration. Risk of Viral Resistance to TPOXX. Updated September 15, 2022. <u>http://dx.doi.org/10.15585/mmwr.mm7137e1</u>



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- O'Laughlin, K MD, et. al. MMWR: Clinical Use of tecovirimat(TPOXX) for the treatment of mpox under and investigational new drug protocol-United States, May-August 2022. 71(37);1190–1195. September, 16, 2022. https://www.cdc.gov/mmwr/volumes/71/wr/mm7137e1.htm?s_cid=mm7137e1_w
- Titanji B, Tegomoh B, Nematollahi S, Konomos M, Kulkarni PA. Mpox A Contemporary Review for Healthcare Professionals. *Open Forum Infectious Diseases*. 2022. <u>https://doi.org/10.1093/ofid/ofac310</u>
- World Health Organization. Clinical Management and Infection Prevention and Control for Mpox - Interim Rapid Response Guidance. June 10, 2022. <u>https://www.who.int/publications/i/item/WHO-MPX-Clinical-and-IPC-2022.1</u>

	Appendix A. Strategic National Stockpile Medical Countermeasures for Treatment					
Name	Indication	Dosing & Administration	Availability	Storage and Handling	Notes	
TPOXX Tecovirimat ST-246	FDA approved for treatment of Smallpox in adults and pediatric patients weighing at least 13kg. Expanded access protocol for mpox	Oral and IV formulations Weight based dosing 14 day course of therapy	SNS request	Oral: 200mg capsules; 42 caps/bottle Stored at controlled room temp IV: 200mg/20mL vial Store refrigerated @ 2- 8°C	TPOXX IV contraindicated in those with severe renal impairment TPOXX oral must be taken within 30 minutes after moderate/high fat meal No human data on use in pregnancy; no toxicity in animal reproductive studies	
<u>Vistide</u> cidofovir	FDA approved for treatment of CMV retinitis in AIDS patients Expanded access protocol for mpox	5mg/kg IV once weekly x 2 weeks Must be administered with fluids and probenecid	Commercially & SNS Request	75 mg/mL in clear glass, single use vial Store at controlled room temperature 20-25°C	Causes severe nephrotoxicity Renal function monitored within 48 hours prior to administration No human data on use in pregnancy; embryotoxic in rats	

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Vaccinia Immune Globulin VIGIV CNJ-016	FDA approved for the treatment of complications associated with vaccinia vaccination Expanded access protocol for mpox	6,000 U/kg IV x 1 dose Higher doses can be given if patient does not respond	SNS Request	15mL vial containing > 50,000 U/vial Product may be stored frozen at or below 5°F (≤ - 15°C) or refrigerated at 36 to 46°F (2 to 8°C)	No animal or human pregnancy data; Other immune globulins used in pregnancy w/o negative effects
TEMBEXA (brincidofovir) CMX001	FDA approved for treatment of Smallpox in adults and pediatric/neonate patients Single patient emergency use investigational new drug (e-IND) protocol	Oral tablet and suspension formulations Adult dose: 2 dose course of 200 mg (2 100 mg tablets) weekly (Day 1 and 8) or 20 mL weekly Weight based dosing; suspension needed for patients <48kg	SNS Request	Tablets: 4 tablets of 100 mg per 1 blister card Suspension: 10 mg/mL; 65 mL per bottle Store at 20°C to 25°C (68°F to 77°F) for tablets/ suspension Avoid contact with broken tablets/suspension Do not crush/divide tablets	May cause fetal harm Perform liver function and pregnancy testing prior to use Do not take with cidofovir Coadministration with OATPB1 and 1B3 inhibitors (includes protease inhibitors for HIV) can increase serum levels of brincidofovir May cause male infertility based on animal models Do not use longer than recommended

Appendix B. Expanded Access IND protocol Information for Tecovirimat.

The information to complete and return to CDC include:

- Informed consent obtained prior to treatment initiation. (Pages 47-51 of IND Protocol)
- Lesion samples for molecular testing from at least 1 lesion prior to tecovirimat treatment, and samples from any new lesions that develop during or up to 7 days after completion of tecovirimat treatment. For <u>CDC Form 50.34</u>, indicate <u>Poxvirus Molecular Detection (CDC-10515)</u> for the test order (code).
- **FDA Form 1572** To be completed by the responsible clinician/healthcare provider overseeing the patient's treatment. Please return within 3 calendar days of tecovirimat treatment initiation along with a CV of the treating physician. This requires an MD or DO license.
- <u>Patient intake form</u> to provide patient's baseline condition at the time of tecovirimat treatment decision. Complete the sections/fields that are applicable to the patient. As possible: if clinical labs (e.g., CBC with differential, UA, metabolic panel) are performed at baseline, please include a copy of the results. Please return within 3 calendar days of tecovirimat treatment to the extent possible. (Pages 55-60 of IND Protocol)
- <u>Adverse event form</u> to report whether any adverse event(s) occurred during treatment with tecovirimat. Return to CDC at the end of patient's tecovirimat treatment course. Life-threatening or serious adverse events during tecovirimat therapy should be reported to CDC within 24 hours of occurrence or as soon as possible. (Page 62 of IND Protocol)
- <u>1 Outpatient Case Report Form</u> (Attachment 2B-Form D in the IND protocol) during tecovirimat therapy (e.g., Day 7) to provide clinical progress of the patient. If clinical labs (e.g., CBC with differential, UA, metabolic panel) can be performed during treatment, please include a copy of the results. (page 64-66 of IND Protocol)
- <u>1 Post Tecovirimat Treatment Form</u> (Attachment 2B-Form E in the IND protocol) to provide patient's clinical outcomes information after completion of treatment. If clinical labs (e.g., CBC with differential, UA, metabolic panel) can be performed at the conclusion of treatment, please include a copy of the results. (page 67-69 of IND Protocol)
- Tecovirimat Product Accountability Form to document product use and/or disposal following completion of treatment. (page 61 of IND Protocol)
- **Photos of lesions**, to the extent possible: at least 1 prior to tecovirimat treatment and 1 during treatment (between days 7 and 14) with dates of the photo(s) indicated. Photo(s) of any new lesions that develop during or up to 7 days after completion of tecovirimat treatment.



Appendix C. Healthcare Provider Ordering Portal (HPOP) Inventory Reporting Guide

Healthcare Provider Ordering Portal (HPOP) Inventory Reporting Guide

How to Report the Number of TPOXX Courses Administered and Available.

IMPORTANT Please consider treating the reporting of therapeutics with the same level of importance as you would control substances. Administrations of TPOXX may be updated daily but must be reported by 5 PM every Tuesday.

Training Scenario: On Friday 8/11 your site received an allocation of 20 courses of TPOXX. On Monday 8/15 of the following week, 2 courses of TPOXX are administered and you have 18 courses remaining at the end of the day Monday. On Tuesday 8/16 you provide an additional 5 courses to patients leaving 14 courses.

MONDAY 8/15 Reporting: 2 administrations and have 18 courses remaining.

Step 1: Login to The Health Partner Order Portal (HPoP) and locate the Therapeutic Inventory section of your site's dashboard.

Courses / Vials Administered and Available					Wastage Save Therapeutic Course	
02) [Monkeypox]				Monkeypox	VX	
100-42) [Monke				Monkeypox	MPXAV	
) NOT USE) (09				Monkeypox	VX	
	02) [Monkeypox] 00-42) [Monke	00-42) [Monke	Administered Available 02) [Monkeypox] 00-42) [Monke	Administered Available History 02) [Monkeypox] 00-42) [Monke	Administered Available History Classifica 02) [Monkeypox] Monkeypox 00-42) [Monke Monkeypox	

MONDAY 8/15 Reporting: Administered 2 courses of TPOXX and have 18 courses remaining. Step 2: In the Courses Administered and Available table.

- A. Select the cell in the Administered column in the TPOXX row and enter 2 as the number of therapeutic courses administered. (Circled in Red Below)
- B. Select the cell in the Available column in the TPOXX row and enter 18 for the number of courses of TPOXX your site would still have available. (Circled in Green Below)
- C. Finally click the Save Therapeutics Courses button to complete the process. (Circled in Orange Below).
- D. The updates are saved and appear in History section of the table. (Circled in Purple Below)
- It may take some time before you see the information displayed in the History section of the table.

Courses / Vials Administered and Available					Wastage C Save Therapeutic Course:	
Jynneos (50632-001-02) [Monkeypox]	А	В		Monkeypox	VX	
TPOXX Oral (50072-200-42) [Monke	2	18		Monkeypox	MPXAV	
Jynneos Test Run (DO NOT USE) (09				Monkeypox	VX	
 For Administered please en (First number in History co For Available please enter 	lumn).					

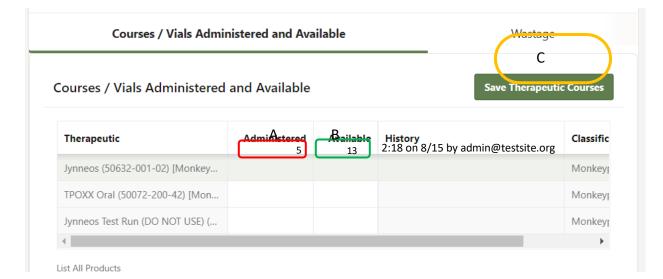
TUESDAY 8/16 Step 1: Login to The Health Partner Order Portal (HPoP) and locate the Therapeutic Inventory section of your site's dashboard. You should now see the inventory you reported on 8/15 in the history section of the Courses Administered and Available table 1:23 on 2/14 by <u>admin@testsite.org</u>. This is read as two courses of TPOXX were administered on 8/15 and 18 courses remain and was reported by <u>admin@testsite.org</u>.

and Available		Save Therapeut	ic Courses
Administered	Available	ዛታ፤ያሪኩ 8/15 by admin@testsite.org	Classifi
			Monkey
			Monkey
	and Available		and Available Save Therapeut

List All Products

TUESDAY 8/16 Step 2: On Tuesday 5 courses were administered and your site has 13 courses still available.

- A. Select the cell in the **Administered** column in the TPOXX row and enter 5 for the number of courses administered on 8/16. (Circled in Red Below) (You do not enter the cumulative number of courses administered only the number the number of courses administered since the last time you reported.)
- Now, select the cell in the Available column in the TPOXX row and enter 13 for the number of courses of TPOXX your site would still have available on 8/16.
 (Circled in Green Below)
- C. Finally click the Save Therapeutics Courses button to complete the process. (Circled in Orange Below). Your new administrations will save and appear in History section of the table. Again, it may take some time before you see your new entry in the History section of the table.



WENDESDAY 8/17: When you login to report administration for Wednesday you will see the administration reported on 8/16 indicating that you administered 5 courses and have 13 remaining.

ourses / Vials Administered	Save	Therapeutic Courses		
Therapeutic	Administered	Available	History 5:13 on 8/16 by admin	Classifi n@testsite.org
Jynneos (50632-001-02) [Monkey				Monkey
TPOXX Oral (50072-200-42) [Mon				Monkey
				Monkey

If you have questions or concerns please contact <u>phpr.nc@dhhs.nc.gov</u> for additional support.

NC DEPARTMENT OF HEALTH AND HUMAN SERVICES • DIVISION OF PUBLIC HEALTH

LOCATION: 5605 Six Forks Road, Building 3, Raleigh, NC 27609 MAILING ADDRESS: 1931 Mail Service Center, Raleigh, NC 27699-1931 www.ncdhhs.gov • TEL: 919-707-5000 • FAX: 919-870-4829

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