Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Patricia A. Yu, Riad Elmor, Kalimah Muhammad, et al. Tecovirimat Use under Expanded Access to Treat Mpox in the United States, 2022–2023. NEJM Evid. DOI: 10.1056/EVIDoa2400189.

SUPPLEMENTARY APPENDIX

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Table S1. Report forms under tecovirimat expanded access investigational new drug (EA-IND) protocol

EA-IND report form	Information collected	Purpose of form	Person completing form	Required or optional	Time at which form is completed	Requested time for form to be returned to CDC
Patient Intake Form[1]	Patient demographics, clinical characteristics of infections, whether orthopoxvirus laboratory testing had been performed, and reasons for tecovirimat treatment. Example questions included: "Number of lesions", "Percent of body affected (%)", "Medical History" with list of pre-existing conditions to select (e.g., HIV/AIDS, atopic dermatitis, leukemia, lymphoma)	Determine clinical features of illnesses for which tecovirimat was prescribed	Clinician	Required	At intake, i.e., at the time tecovirimat was prescribed	Within 7 days of prescribing tecovirimat treatment[2]
Clinical Outcome Form[1,3]	Lesion progression, hospitalization, time to subjective improvement, level of improvement at treatment completion, and whether serious adverse events (SAE)[4] had occurred with tecovirimat treatment. Example questions included: "What was the outcome of the patient?", "Was patient hospitalized after tecovirimat initiation", "Signs/symptoms first started to improve on tecovirimat treatment day #".	Elucidate potential role of tecovirimat by understanding outcomes experienced by treated patients and reported serious adverse events	Clinician	Required until August 2022. Optional from August 2022 through June 2023. Reverted to being required starting in June 2023[3]	During treatment (Day 1–7 and 8–14) and post-treatment (after completion of tecovirimat treatment)[5]	7 days of last patient follow-up after the last dose of tecovirimat[5]
MedWatch[6]	SAEs and selected AEs of interest[4] during or after tecovirimat initiation	Characterize severe adverse events and adverse events of interest	Clinician	Required	At the time that an SAE or selected AE of interest is reported to a clinician	Within 3 days of treating clinician's awareness of SAE/selected AE[7]
Patient Diary	Clinical improvement, as perceived by the patient, via documentation of daily progress and outcomes at completion of treatment and 7 days later	Elucidate potential role of tecovirimat by understanding day-to-day clinical improvement, from patient's perspective, during and after tecovirimat treatment	Patient	Optional	7 days after the last dose of tecovirimat[8]	7 days after the last dose of tecovirimat[8]

1 Treating clinicians could supplement data in completed EA-IND forms with progress notes from patients' electronic health records (EHR) with submission of earlier versions of the intake and clinical outcome forms, prior to availability starting October 28, 2022 of a web-based EA-IND online registry and report forms. Free-text fields in the forms facilitated sharing of additional information that clinicians deemed important to our understanding of individual cases.

2 Patient intake form Version 5.1 (dated May 2022) was required to be completed prior to the first dose of tecovirimat. Version 6.0 (dated July 2022) was required to be completed & returned within 3 working days of initiation of tecovirimat. Version 6.1 (dated August 2022) was required to be completed & returned within 7 calendar days of initiation of tecovirimat. Version 6.2 (dated October 2022) was required to be completed & returned no later than 7 calendar days of initiation of tecovirimat.

3 The clinical outcome form was required under the EA-IND from May to August 2022. To alleviate the reporting burden in response to providers and other stakeholders expressing challenges with upholding all EA-IND reporting requirements during the mpox outbreak, the clinical outcome form was made optional starting in August 2022. It reverted to being required in June 2023.

4 Serious adverse events (SAE) were defined as death, life-threatening AE, inpatient hospitalization, or prolongation of existing hospitalization, persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions; congenital anomaly/birth defect; an important medical event that based on appropriate medical judgement may jeopardize the patient and may require medical or surgical intervention to prevent one of the aforementioned outcomes. Selected AEs of interest included seizure, tremor and/or tingling sensation, purpura, renal function abnormalities, or hepatic function abnormalities.

5 Clinical outcome form Version 5.1 (dated May 2022) was to be completed at least once during tecovirimat treatment, and 7 days and 30 days after the last dose of tecovirimat. Version 6.0 (dated July 2022) was to be completed during tecovirimat treatment (Day 1–7 and 8–14) and 7–10 days after the last dose of tecovirimat. Form was to be returned within 3 working days of last patient follow-up. Version 6.1 (dated August 2022) was to be completed 3–14 calendar days after the last dose of tecovirimat. Form was to be returned within 7 calendar days of last patient follow-up. Version 6.2 (dated October 2022) was to be completed 3–14 calendar days after the last dose of tecovirimat. Form was to be returned within 7 calendar days of last patient follow-up.

6 SAEs and selected adverse events were reported via the MedWatch form and Clinical Outcome form.

7 SAEs were required to be reported under the EA-IND across all protocol versions via the clinical outcome form. The MedWatch form for reporting SAEs to CDC was introduced starting in July 2022. Selected AEs were individually identified as AEs to be reported to CDC starting with Version 6.2 (dated October 2022). Regardless of inclusion of the clinical outcome form, SAEs and AEs of interest were expected to be reported to MedWatch.

8 Patient diary Version 5.1 (dated May 2022) was to be completed daily during treatment and through the last dose of tecovirimat (Day 1–14). Form was requested to be returned in a "timely manner (within 3–5 days)". Version 6.0 (dated July 2022) was to be completed daily during treatment and through the last dose of tecovirimat (Day 1–14) and 7 days after the last dose of tecovirimat. Form was requested to returned to CDC with no required specified return-by date ("When you have completed this form, please send to CDC.")

Table S2. Demographic and clinical characteristics and outcomes by baseline categorical number of lesions among patients with severe immunocompromise or atopic dermatitis/conditions affecting skin integrity

	0–9 lesions no. (%)	10–100 lesions no. (%)	Greater than 100 lesions no. (%)
	Patients with severe immunocompromise (n=51)		
CLINICAL CHARACTERISTICS AND OUTCOMES — no. patients	**11**	**38**	**2**
Race — no. (%)			
White	4 (36.4%)	13 (34.2%)	1 (50.0%)
African American/Black	5 (45.5%)	21 (55.3%)	1 (50.0%)
Asian	0 (0.0%)	2 (5.3%)	0 (0.0%)
Other	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unknown	2 (18.2%)	2 (5.3%)	0 (0.0%)
Time from illness onset to tecovirimat prescribed[1] — no. patients	10	31	2
Median (IQR) — days	9.5 (7.0–20.0)	10.0 (5.5–15.0)	13.0 (10.5–15.5)
Percent body affected by lesions — no. (%)			
0% to <10%	4 (36.4%)	9 (23.7%)	0 (0.0%)
10% to <25%	2 (18.2%)	7 (18.4%)	0 (0.0%)
25% to <50%	1 (9.1%)	2 (5.3%)	0 (0.0%)
50% to <75%	0 (0.0%)	6 (15.8%)	1 (50.0%)
75% to 100%	0 (0.0%)	2 (5.3%)	1 (50.0%)
Unknown	4 (36.4%)	12 (31.6%)	0 (0.0%)
Duration of tecovirimat treatment — no. (%)			
< 14 days	2 (18.2%)	3 (7.9%)	0 (0.0%)
Shorter therapy due to symptom resolution	1/2 (50%)	0/3 (0%)	0/0 (0.0%)
Shorter therapy due to adverse event	0/2 (0%)	2/3 (66.7%)	0/0 (0.0%)
14 days	8 (72.7%)	14 (36.8%)	1 (50.0%)

	0–9 lesions no. (%)	**10–100 lesions no. (%)**	**Greater than 100 lesions no. (%)**
> 14 days	1 (9.1%)	20 (52.6%)	1 (50.0%)
Unknown	0 (0.0%)	1 (2.6%)	2 (100.0%)
Duration of tecovirimat treatment — no. patients	11	37	2
Range (median) (IQR)	1–70 days (14 days) (IQR 14–14 days)	1.0–108.0 days (17.0 days) (IQR 14.0–35.0 days)	14.0–110.0 days (62.0 days) (IQR 38.0–86.0 days)
Tecovirimat route of administration — no. (%)			
Oral	10 (90.9%)	19 (50.0%)	1 (50.0%)
NG tube	1/10 (10%)	2/19 (10.5%)	0/1 (0%)
Intravenous[2]	1 (9.1%)	19 (50.0%)	1 (50.0%)
Unknown	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hospitalization status at baseline — no. (%)			
Outpatient	6 (54.5%)	22 (57.9%)	1 (50.0%)
Inpatient	3 (27.3%)	12 (31.6%)	1 (50.0%)
Intensive care unit	1/3 (33.3%)	2/12 (16.7%)	0/1 (0%)
Unknown	2 (18.2%)	4 (10.5%)	0 (0.0%)
Hospitalization after tecovirimat initiation among patients treated as outpatients at baseline — no. (%)			
Yes	0/6 (0.0%)	14/22 63.6%	0/1 0.0%
Intensive care unit	0/0 0.0%	2/14 (14.3%)	0/0 0.0%
No	5/6 (83.3%)	8/22 (36.4%)	1/1 (100.0%)
Unknown	1/6 (16.7%)	0/22 (0.0%)	0/1 (0.0%)
Days from tecovirimat initiation to subjective improvement[3] — no. patients	6	20	1
Median (IQR)	2.5 (2.0–3.8)	4.0 (3.0–7.0)	7.0 (7.0–7.0)

	0–9 lesions no. (%)	10–100 lesions no. (%)	Greater than 100 lesions no. (%)
Recovery status — no. (%)			
Recovered without sequelae	7 (63.6%)	7 (18.4%)	1 (50.0%)
Recovered with sequelae	0 (0.0%)	5 (13.2%)	0 (0.0%)
Not recovered	2 (18.2%)	10 (26.3%)	1 (50.0%)
Death	2 (18.2%)	16 (42.1%)	0 (0.0%)
Unknown	0 (0.0%)	0 (0.0%)	0 (0.0%)
Days from tecovirimat initiation to recovery — no. patients	3	2	1
Median (IQR)	10.0 (10.0–15.5)	30.5 (23.3–37.8)	10.0 (10.0–10.0)
New lesions developed after tecovirimat initiation — no. (%)			
Yes	2 (18.2%)	8 (21.1%)	0 (0.0%)
No	8 (72.7%)	19 (50.0%)	1 (50.0%)
Unknown	1 (9.1%)	11 (28.9%)	1 (50.0%)
Unresolved lesions still present after completion of tecovirimat treatment — no. (%)			
Yes	3 (27.3%)	17 (44.7%)	0 (0.0%)
No	6 (54.5%)	6 (15.8%)	1 (50.0%)
Unknown	2 (18.2%)	15 (39.5%)	1 (50.0%)
Number of lesions present after treatment completion — no. (%)			
0 lesions	4 (36.4%)	4 (10.5%)	0 (0.0%)
1 to 9 lesions	5 (45.5%)	18 (47.4%)	2 (100.0%)
10 to 100 lesions	0 (0.0%)	9 (23.7%)	0 (0.0%)
> 100 lesions	0 (0.0%)	2 (5.3%)	0 (0.0%)

	0–9 lesions no. (%)	10–100 lesions no. (%)	Greater than 100 lesions no. (%)
Unknown	2 (18.2%)	5 (13.2%)	0 (0.0%)
Number of lesions at posttreatment — no. patients	6	22	0
Median (IQR)	0.5 (0–4.0)	9.0 (1.8–27.5)	–
	Atopic dermatitis or condition affecting skin integrity (no documented severe immunocompromise) (n=46)		
CLINICAL CHARACTERISTICS AND OUTCOMES — no. patients	**21**	**21**	**4**
Race — no. (%)			
White	10 (47.6%)	10 (47.6%)	2 (50.0%)
African American/Black	8 (38.1%)	5 (23.8%)	2 (50.0%)
Asian	1 (4.8%)	0 (0.0%)	0 (0.0%)
Other	1 (4.8%)	4 (19.0%)	0 (0.0%)
Unknown	1 (4.8%)	2 (9.5%)	0 (0.0%)
Time from illness onset to tecovirimat prescribed[1] — no. patients	19	21	4
Median (IQR) — days	6.0 (4.5–9.0)	8.0 (7.0–12.0)	5.5 (5.0–11.3)
Percent body affected by lesions — no. (%)			
0% to <10%	15 (71.4%)	10 (47.6%)	0 (0.0%)
10% to <25%	1 (4.8%)	1 (4.8%)	0 (0.0%)
25% to <50%	0 (0.0%)	2 (9.5%)	0 (0.0%)
50% to <75%	0 (0.0%)	1 (4.8%)	1 (25.0%)
75% to 100%	0 (0.0%)	2 (9.5%)	0 (0.0%)
Unknown	5 (23.8%)	5 (23.8%)	3 (75.0%)
Duration of tecovirimat treatment — no. (%)			
< 14 days	0 (0.0%)	2 (9.5%)	0 (0.0%)

	0–9 lesions no. (%)	10–100 lesions no. (%)	Greater than 100 lesions no. (%)
Shorter therapy due to symptom resolution	0/0 (0.0%)	1/2 (50%)	0/0 (0.0%)
Shorter therapy due to adverse event	0/0 (0.0%)	1/2 (50%)	0/0 (0.0%)
14 days	17 (81.0%)	19 (90.5%)	4 (100.0%)
> 14 days	2 (9.5%)	0 (0.0%)	0 (0.0%)
Unknown	2 (9.5%)	0 (0.0%)	0 (0.0%)
Duration of tecovirimat treatment — no. patients			
Range (median) (IQR)	14.0–26.0 days (14.0 days) (IQR 14.0–14.0 days)	7.0–14.0 days (14.0 days) (IQR 14.0–14.0 days)	14.0–14.0 days (14.0 days) (IQR 14.0–14.0 days)
Tecovirimat route of administration — no. (%)			
Oral	21 (100.0%)	21 (100.0%)	4 (100.0%)
NG tube	0/21 (0%)	0/21 (0%)	0/4 (0%)
Intravenous	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unknown	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hospitalization status at baseline — no. (%)			
Outpatient	20 (95.2%)	17 (81.0%)	0 (0.0%)
Inpatient	0 (0.0%)	1 (4.8%)	0 (0.0%)
Intensive care unit	0/0 (0.0%)	0/1 (0.0%)	0/0 (0.0%)
Unknown	1 (4.8%)	3 (14.3%)	4 (100.0%)
Hospitalization after tecovirimat initiation among patients treated as outpatients at baseline — no. (%)			
Yes	0/20 (0.0%)	1/17 (5.9%)	0/0 (0.0%)
Intensive care unit	0/0 (0.0%)	0/1 (0.0%)	0/0 (0.0%)
No	20/20 (100.0%)	15/17 (88.2%)	0/0 (0.0%)
Unknown	0/20 (0.0%)	1/17 (5.9%)	0/0 (0.0%)

	0–9 lesions no. (%)	10–100 lesions no. (%)	Greater than 100 lesions no. (%)
Days from tecovirimat initiation to subjective improvement — no. patients	19	18	3
Median (IQR)	3.0 (3.0–4.0)	3.0 (2.0–4.0)	4.0 (3.0–4.5)
Recovery status — no. (%)			
Recovered without sequelae	19 (90.5%)	14 (66.7%)	3 (75.0%)
Recovered with sequelae	1 (4.8%)	6 (28.6%)	1 (25.0%)
Not recovered	1 (4.8%)	1 (4.8%)	0 (0.0%)
Death	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unknown	0 (0.0%)	0 (0.0%)	0 (0.0%)
Days from tecovirimat initiation to recovery — no. patients	10	9	0
Median (IQR)	12.0 (11.3–13.0)	13.0 (10.0–14.0)	–
New lesions developed after tecovirimat initiation — no. (%)			
Yes	2 (9.5%)	4 (19.0%)	1 (25.0%)
No	19 (90.5%)	14 (66.7%)	2 (50.0%)
Unknown	0 (0.0%)	3 (14.3%)	1 (25.0%)
Unresolved lesions still present after completion of tecovirimat treatment — no. (%)			
Yes	3 (14.3%)	4 (19.0%)	2 (50.0%)
No	16 (76.2%)	12 (57.1%)	2 (50.0%)
Unknown	2 (9.5%)	5 (23.8%)	0 (0.0%)
Number of lesions present after treatment completion — no. (%)			

	0–9 lesions no. (%)	10–100 lesions no. (%)	Greater than 100 lesions no. (%)
0 lesions	12 (57.1%)	7 (33.3%)	2 (50.0%)
1 to 9 lesions	7 (33.3%)	7 (33.3%)	1 (25.0%)
10 to 100 lesions	0 (0.0%)	1 (4.8%)	1 (25.0%)
> 100 lesions	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unknown	2 (9.5%)	6 (28.6%)	0 (0.0%)
Number of lesions at posttreatment — no. patients	16	9	4
Median (IQR)	0.0 (0.0–0.3)	0.0 (0.0–0.0)	0.5 (0.0–5.8)

1 Time from illness onset to when tecovirimat was prescribed calculated based on availability of illness onset before date of tecovirimat initiation. Tecovirimat initiation date is defined as date of tecovirimat administration, date tecovirimat was prescribed, or date of assessment/date of intake form, in priority order.

2 Among patients with severe immunocompromise, 12 patients with 10–100 lesions at baseline and 1 patient with greater than 100 lesions at baseline received oral and IV tecovirimat.

3 Multiple iterations of this question were asked across three versions of the clinical outcome form. The July 2022 (v6.0) clinical outcome form defined this as “Time to first observed (including patient-reported) improvement - Signs/symptoms first started to improve on Tecovirimat treatment day #”. The August 2022 (v6.1) clinical outcome form defined this as “Lesions or pain first started to improve on TPOXX treatment day #”. The October 2022 (v6.2) clinical outcome form defined this as “Lesions first started to improve on tecovirimat treatment day #”.

Table S3. Demographic and clinical characteristics and outcomes by baseline categorical number of lesions, among patients with HIV <200 cells/mm^3 and ≥ 200 cells/mm^3

	0–9 lesions no. (%)	10–100 lesions no. (%)	Greater than 100 lesions no. (%)	0–9 lesions no. (%)	10–100 lesions no. (%)	Greater than 100 lesions no. (%)
	Patients with HIV CD4 <200 cells/mm^3 (n=43)			Patients with HIV CD4 ≥200 cells/mm^3, excluding severe immunocompromise (n=61)		
CLINICAL CHARACTERISTICS AND OUTCOMES — no. patients	**9**	**32**	**2**	**25**	**34**	**2**
Race — no. (%)						
White	4 (44.4%)	9 (28.1%)	1 (50.0%)	11 (44.0%)	10 (29.4%)	0 (0.0%)
African American/Black	3 (33.3%)	18 (56.3%)	1 (50.0%)	4 (16.0%)	10 (29.4%)	0 (0.0%)
Asian	0 (0.0%)	2 (6.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (16.0%)	2 (5.9%)	0 (0.0%)
Unknown	2 (22.2%)	3 (9.4%)	0 (0.0%)	6 (24.0%)	12 (35.3%)	2 (100.0%)
Time from illness onset to tecovirimat prescribed[1] — no. patients	8	26	2	24	34	2
Median (IQR) — days	7.0 (7.0–21.3)	10.0 (6.0–19.0)	13.0 (10.5–15.5)	7.5 (6.0–11.3)	7.0 (5.0–9.0)	7.5 (6.3–8.8)
Percent body affected by lesions — no. (%)						
0% to <10%	3 (33.3%)	8 (25.0%)	0 (0.0%)	13 (52.0%)	4 (11.8%)	0 (0.0%)
10% to <25%	1 (11.1%)	6 (18.8%)	0 (0.0%)	0 (0.0%)	7 (20.6%)	0 (0.0%)
25% to <50%	1 (11.1%)	2 (6.3%)	0 (0.0%)	0 (0.0%)	1 (2.9%)	0 (0.0%)
50% to <75%	0 (0.0%)	3 (9.4%)	1 (50.0%)	0 (0.0%)	2 (5.9%)	0 (0.0%)
75% to 100%	0 (0.0%)	2 (6.3%)	1 (50.0%)	0 (0.0%)	1 (2.9%)	0 (0.0%)
Unknown	4 (44.4%)	11 (34.4%)	0 (0.0%)	12 (48.0%)	19 (55.9%)	2 (100.0%)
Duration of tecovirimat treatment — no. (%)						
< 14 days	1 (11.1%)	2 (6.3%)	0 (0.0%)	3 (33.3%)	3 (9.4%)	0 (0.0%)
Shorter therapy due to symptom resolution	1/1 (100%)	0/2 (0%)	0/0 (0.0%)	1/3 (33.3%)	2/3 (66.7%)	0/0 (0.0%)
Shorter therapy due to adverse event	0/1 (0%)	2/2 (100%)	0/0 (0.0%)	1/3 (33.3%)	2/3 (66.7%)	0/0 (0.0%)
14 days	6 (66.7%)	9 (28.1%)	1 (50.0%)	14 (155.6%)	18 (56.3%)	0 (0.0%)
> 14 days	1 (11.1%)	19 (59.4%)	1 (50.0%)	0 (0.0%)	2 (6.3%)	0 (0.0%)

	0–9 lesions no. (%)	10–100 lesions no. (%)	Greater than 100 lesions no. (%)	0–9 lesions no. (%)	10–100 lesions no. (%)	Greater than 100 lesions no. (%)
	Patients with HIV CD4 <200 cells/mm^3 (n=43)			Patients with HIV CD4 ≥200 cells/mm^3, excluding severe immunocompromise (n=61)		
Unknown	1 (11.1%)	2 (6.3%)	0 (0.0%)	8 (88.9%)	11 (34.4%)	2 (100.0%)
Duration of tecovirimat treatment — no. patients	9	31	2	23	33	2
Range (median) (IQR)	10.0–70.0 (14.0) (IQR 14.0–14.0)	5.0–108.0 days (21.0 days) (IQR 14.0–36.5 days)	14.0–110.0 (62.0) (IQR 38.0–86.0)	5.0–14.0 days (14.0 days) (IQR 14.0–14.0 days)	3.0–19.0 days (14.0 days) (IQR 14.0–14.0 days)	14.0–14.0 days (14.0 days) (IQR 14.0–14.0 days)
Tecovirimat route of administration — no. (%)						
Oral	8 (88.9%)	14 (43.8%)	1 (50.0%)	19 (76.0%)	21 (61.8%)	0 (0.0%)
NG tube	0/8 (0%)	2/14 (14.3%)	0/1 (0%)	0/19 (0%)	1/21 (4.8%)	0/0 (0.0%)
Intravenous[2]	0 (0.0%)	17 (53.1%)	1 (50.0%)	0 (0.0%)	2 (5.9%)	0 (0.0%)
Unknown	1 (11.1%)	1 (3.1%)	0 (0.0%)	6 (24.0%)	11 (32.4%)	2 (100.0%)
Hospitalization status at baseline — no. (%)						
Outpatient	6 (66.7%)	19 (59.4%)	1 (50.0%)	18 (72.0%)	17 (50.0%)	0 (0.0%)
Inpatient	2 (22.2%)	10 (31.3%)	1 (50.0%)	1 (4.0%)	6 (17.6%)	0 (0.0%)
Intensive care unit	0/2 (0%)	1/10 (10%)	0/1 (0%)	0/1 (0.0%)	1/6 (0.0%)	0/0 (0.0%)
Unknown	1 (11.1%)	3 (9.4%)	0 (0.0%)	6 (24.0%)	11 (32.4%)	2 (100.0%)
Hospitalization after tecovirimat initiation among patients treated as outpatients at baseline — no. (%)						
Yes	0/6 (0%)	13/19 (68.4%)	0/1 (0%)	0/18 (0.0%)	1/17 (5.9%)	0/0 (0.0%)
Intensive care unit	0/0 (0%)	2/13 (15.4%)	0/0 (0%)	0/0 (0.0%)	0/1 (0.0%)	0/0 (0.0%)
No	5/6 (83.3%)	6/19 (31.6%)	1/1 (100.0%)	17/18 (94.4%)	15/17 (88.2%)	0/0 (0.0%)
Unknown	1/6 (16.7%)	0/19 (0%)	0/1 (0%)	1/18 (5.6%)	1/17 (5.9%)	0/0 (0.0%)
Days from tecovirimat initiation to subjective improvement[3] — no. patients	6	15	1	21	30	1

	0–9 lesions no. (%)	10–100 lesions no. (%)	Greater than 100 lesions no. (%)	0–9 lesions no. (%)	10–100 lesions no. (%)	Greater than 100 lesions no. (%)
	Patients with HIV CD4 <200 cells/mm^3 (n=43)			Patients with HIV CD4 ≥200 cells/mm^3, excluding severe immunocompromise (n=61)		
Median (IQR)	2.5 (2.0–3.8)	5.0 (3.5–7.0)	7.0 (7.0–7.0)	3.0 (2.0–3.0)	3.0 (2.0–4.0)	3.0 (3.0–3.0)
Recovery status — no. (%)						
Recovered without sequelae	5 (55.6%)	4 (12.5%)	1 (50.0%)	17 (68.0%)	20 (58.8%)	0 (0.0%)
Recovered with sequelae	0 (0.0%)	5 (15.6%)	0 (0.0%)	2 (8.0%)	1 (2.9%)	0 (0.0%)
Not recovered	2 (22.2%)	7 (21.9%)	1 (50.0%)	0 (0.0%)	2 (5.9%)	0 (0.0%)
Death	1 (11.1%)	15 (46.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unknown	1 (11.1%)	1 (3.1%)	0 (0.0%)	6 (24.0%)	11 (32.4%)	2 (100.0%)
Days from tecovirimat initiation to recovery — no. patients	3	2	1	11	14	0
Median (IQR)	10.0 (10.0–15.5)	30.5 (23.3–37.8)	10.0 (10.0–10.0)	9.0 (2.5–11.0)	7.0 (4.3–14.0)	--
New lesions developed after tecovirimat initiation — no. (%)						
Yes	2 (22.2%)	7 (21.9%)	0 (0.0%)	4 (16.0%)	2 (5.9%)	0 (0.0%)
No	6 (66.7%)	13 (40.6%)	1 (50.0%)	15 (60.0%)	16 (47.1%)	0 (0.0%)
Unknown	1 (11.1%)	12 (37.5%)	1 (50.0%)	6 (24.0%)	16 (47.1%)	2 (100.0%)
Unresolved lesions still present after completion of tecovirimat treatment — no. (%)						
Yes	2 (22.2%)	15 (46.9%)	0 (0.0%)	2 (8.0%)	2 (5.9%)	0 (0.0%)
No	5 (55.6%)	4 (12.5%)	1 (50.0%)	13 (52.0%)	16 (47.1%)	0 (0.0%)
Unknown	2 (22.2%)	13 (40.6%)	1 (50.0%)	10 (40.0%)	16 (47.1%)	2 (100.0%)
Number of lesions present after treatment completion — no. (%)						
0 lesions	3 (33.3%)	2 (6.3%)	0 (0.0%)	5 (20.0%)	11 (32.4%)	0 (0.0%)
1 to 9 lesions	4 (44.4%)	16 (50.0%)	2 (100.0%)	9 (36.0%)	7 (20.6%)	0 (0.0%)

	0–9 lesions no. (%)	10–100 lesions no. (%)	Greater than 100 lesions no. (%)	0–9 lesions no. (%)	10–100 lesions no. (%)	Greater than 100 lesions no. (%)
	Patients with HIV CD4 <200 cells/mm^3 (n=43)			Patients with HIV CD4 ≥200 cells/mm^3, excluding severe immunocompromise (n=61)		
10 to 100 lesions	0 (0.0%)	8 (25.0%)	0 (0.0%)	0 (0.0%)	1 (2.9%)	0 (0.0%)
> 100 lesions	0 (0.0%)	2 (6.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unknown	2 (22.2%)	4 (12.5%)	0 (0.0%)	11 (44.0%)	15 (44.1%)	2 (100.0%)
Number of lesions at posttreatment — no. patients	5	16	0	12	24	2
Median (IQR)	0.5 (0.0–2.0)	10.0 (3.3–27.5)	–	0.0 (0.0–0.0)	0.0 (0.0–3.0)	0.0 (0.0–0.0)

1 Time from illness onset to when tecovirimat was prescribed calculated based on availability of illness onset before date of tecovirimat initiation. Tecovirimat initiation date is defined as date of tecovirimat administration, date tecovirimat was prescribed, or date of assessment/date of intake form, in priority order.

2 Among patients with HIV CD4 <200 cells/mm^3, 11 patients with 10–100 lesions at baseline and 1 patient with greater than 100 lesions at baseline received oral and IV tecovirimat. Among patients with HIV CD4 ≥200 cells/mm^3, 6 patients with 10–100 lesions at baseline received oral and IV tecovirimat.

3 Multiple iterations of this question were asked across three versions of the clinical outcome form. The July 2022 (v6.0) clinical outcome form defined this as “Time to first observed (including patient-reported) improvement - Signs/symptoms first started to improve on Tecovirimat treatment day #”. The August 2022 (v6.1) clinical outcome form defined this as “Lesions or pain first started to improve on TPOXX treatment day #”. The October 2022 (v6.2) clinical outcome form defined this as “Lesions first started to improve on tecovirimat treatment day #”.

Table S4. Tecovirimat treatment among patients treated intravenously[1] as reported in the clinical outcome form containing posttreatment completion information: summary of baseline characteristics and outcomes (n=33)

	Patients treated with intravenous tecovirimat and having matching intake and outcome forms (n=33)[1]
BASELINE AND CLINICAL CHARACTERISTICS	
Immunocompromised status — no. (%)	
Severe immunocompromise[2]	21 (63.6%)
HIV CD4 count >200 cells/mm^3	2 (6.1%)
HIV Unknown CD4 count	6 (18.2%)
No documented condition causing severe immunocompromise[3]	4 (12.1%)
Sex assigned at birth — no. (%)	
Male	33 (100.0%)
Female	0 (0.0%)
Gender identity — no. (%)	
Male	31 (93.9%)
Female	0 (0.0%)
Transgender female	1 (3.0%)
Transgender male	0 (0.0%)
Other	1 (3.0%)
Unknown	0 (0.0%)
Median age (IQR) — no. (%)	37.0 (33.0–41.0)
Age group — no. (%)	
< 18 years	0 (0.0%)
18 to < 65 years	33 (100.0%)
≥ 65 years	0 (0.0%)
Ethnicity — no. (%)	
Hispanic or Latino	3 (9.1%)
Not Hispanic or Latino	25 (75.8%)
Unknown	5 (15.2%)
Race — no. (%)	
White	9 (27.3%)
African American/Black	20 (60.6%)
American Indian or Alaska Native	1 (3.0%)
Other	1 (3.0%)

Unknown	2 (6.1%)
History of smallpox or mpox vaccination[4] — no. (%)	
Yes	2 (6.1%)
No	26 (78.8%)
Unknown	5 (15.2%)
Time from illness onset to tecovirimat prescribed[5]	27
Median (IQR) — days	8.0 (4.5–13.0)
Percent body affected by lesions	
0% to <10%	7 (21.2%)
10% to <25%	10 (30.3%)
25% to <50%	2 (6.1%)
50% to <75%	5 (15.2%)
75% to 100%	1 (3.0%)
Unknown	8 (24.2%)
Reason for tecovirimat treatment (not mutually exclusive)[6] — no (%)	
Lesions in anatomic areas that might result in serious sequelae	22/29 (75.9%)
Pain	14/29 (48.3%)
At risk for severe disease due to one more conditions	25/29 (86.2%)
Severe infection	1/4 (25.0%)
Other	1/29 (3.4%)
Signs and symptoms documented at start of treatment[7] (not mutually exclusive) — no (%)	
Rash	13/14 (92.9%)
Pain	6/14 (42.9%)
Lymphadenopathy	2/14 (14.3%)
Fever	4/14 (28.6%)
Distribution of lesions — no (%)	
Skin	31/32 (96.9%)
Anogenital	20/32 (62.5%)
Oral mucosa	11/32 (34.4%)
Ocular	3/32 (9.4%)
Hospitalization status at baseline	
Outpatient	16 (48.5%)
Inpatient	14 (42.4%)
Intensive care unit	4/14 (28.6%)
Unknown	3 (9.1%)

CLINICAL OUTCOMES	
Duration of tecovirimat treatment — no. (%)	
< 14 days	3 (9.1%)
Shorter therapy due to adverse event	2/3 (66.7%)
14 days	8 (24.2%)
> 14 days	21 (63.6%)
Duration of tecovirimat treatment — range (median) (IQR)	1.0–108.0 days (21.0 days) (IQR 14.0–38.0days)
Hospitalization after tecovirimat initiation among patients treated as outpatients at baseline — no. (%)	
Yes	16/16 (100%)
Intensive care unit	4/16 (25%)
No	0/16 (0%)
Unknown	0/16 (0%)
Days from tecovirimat initiation to subjective improvement[8], n	16
Median (IQR)	5.0 days (4.5–7.8 days)
Recovery status — no. (%)	
Recovered without sequelae	7 (21.2%)
Recovered with sequelae	3 (9.1%)
Not recovered	8 (24.2%)
Death	15 (45.5%)
Days from tecovirimat initiation to recovery, n	4
Median (IQR)	14.0 days (13.8–21.8 days)
New lesions developed after tecovirimat initiation — no. (%)	
Yes	11 (33.3%)
No	12 (36.4%)
Unknown	10 (30.3%)
Unresolved lesions still present after completion of tecovirimat treatment — no. (%)	
Yes	13 (39.4%)
No	5 (15.2%)
Unknown	15 (45.5%)
Number of lesions present after treatment completion	
0 lesions	4 (12.1%)
1 to 9 lesions	17 (51.5%)

10 to 100 lesions	8 (24.2%)
> 100 lesions	2 (6.1%)
Unknown	2 (6.1%)
Number of lesions at posttreatment, n	19
Median (IQR)	10.0 days (1.5–40.0 days)

1 Includes patients treated with intravenous tecovirimat prior to or following oral tecovirimat. Restricted to patients with matching intake form and outcome form containing posttreatment completion information.

2 Patients with severe immunocompromise treated with intravenous tecovirimat had HIV with CD4 count <200 cells/mm^3 (n=19) and patients with history of solid organ transplant (n=2).

3 Excludes patients with HIV, atopic dermatitis, or other condition affecting skin integrity.

4 Vaccination with one or two doses of Jynneos during the 2022–2023 mpox outbreak. Timeframe of vaccination in relation to exposure among patients with available data for date of exposure and date of vaccination. Patients with history of smallpox vaccination before the outbreak are excluded.

5 Time from illness onset to when tecovirimat was prescribed calculated based on availability of illness onset before date of tecovirimat initiation. Tecovirimat initiation date is defined as date of tecovirimat administration, date tecovirimat was prescribed, or date of assessment/date of intake form, in priority order.

6 Reasons for tecovirimat treatment that included risk of severe outcome due to immunosuppression, lesions in sensitive anatomical areas, pain, and other were queried on the intake form starting with version 6.0 dated July 2022. With version 6.2 dated October 2022, the risk category was revised to risk of severe outcome due to uncontrolled HIV or other conditions, pregnancy, pediatric patient, or condition affecting skin integrity and a new category added for severe infections (e.g., large number of lesions such that they are confluent; sepsis; encephalitis). Severe infection was not systematically captured in free-text field for the “Other” category in forms returned prior to version 6.2 dated October 2022, which did not include a specific option for severe infection.

7 Signs/symptoms started to be queried in the patient intake form version dated August 2022 and included categories for rash, pain, and lymphadenopathy. Additional categories of proctitis, abscess, cellulitis, dysuria, headache, malaise, and shortness of breath were added to the intake form version dated October 2022. Only patients with non-missing data and at least one reason are included. Form does not distinguish absence of symptom from unknown symptom status.

8 Multiple iterations of this question were asked across three versions of the clinical outcome form. The July 2022 (v6.0) clinical outcome form defined this as “Time to first observed (including patient-reported) improvement - Signs/symptoms first started to improve on Tecovirimat treatment day #”. The August 2022 (v6.1) clinical outcome form defined this as “Lesions or pain first started to improve on TPOXX treatment day #”. The October 2022 (v6.2) clinical outcome form defined this as “Lesions first started to improve on tecovirimat treatment day #”.

Table S5. History of Jynneos vaccination among patients prescribed tecovirimat May 29, 2022–July 10, 2023, by cohort (N=7,181)

	All patients (N=7,181)	HIV excluding CD4 < 200 cells/mm^3 and other severe immunocompromise (n=3,413)	Severely immuno-compromised (n=310)	Atopic dermatitis or other skin condition (no documented severe immunocompromise) (n=299)	Pediatric patients <18 years (n=29)
History of at least partial vaccination (at least one dose of Jynneos vaccination administered since 5/22/2022)—no. (%)	846	337	16	57	0
Before mpox exposure					
≥ 15 days before exposure	73/846 (8.6%)	26/337 (7.7%)	0/16 (0%)	12/57 (21.1%)	0 (0%)
1–14 days before exposure	55/846 (6.5%)	20/337 (5.9%)	1/16 (6.3%)	3/57 (5.3%)	0 (0%)
After mpox exposure					
0–4 days after exposure	91/846 (10.8%)	38/337 (11.3%)	1/16 (6.3%)	7/57 (12.3%)	0 (0%)
5–14 days after exposure	119/846 (14.1%)	45/337 (13.4%)	0/16 (0%)	4/57 (7%)	0 (0%)
≥ 15 days after exposure	20/846 (2.4%)	8/337 (2.4%)	1/16 (6.3%)	0/57 (0%)	0 (0%)
Unknown timing	488/846 (57.7%)	200/337 (59.3%)	13/16 (81.3%)	31/57 (54.4%)	0 (0%)

Table S6. Number of lesions at baseline by timing of at least one dose of Jynneos vaccine relative to reported mpox exposure

	Vaccination BEFORE mpox exposure		**Vaccination AFTER mpox exposure**			**Unknown timing**
	Vaccinated ≥15 days before mpox exposure	Vaccinated 1–14 days before mpox exposure	Vaccinated 0–4 days after mpox exposure	Vaccinated 5–14 days after mpox exposure	Vaccinated ≥15 days after mpox exposure	
Approximate number of lesions						
No. patients	33	19	30	32	6	147
Median no. lesions (IQR)	7.0 (3.0–14.0)	11.0 (7.0–25.0)	15.0 (5.0–25.0)	15.0 (10.0–25.0)	15.0 (9.0–18.8)	10.0 (4.0–20.0)
Categorical number of lesions — no. (%)						
0-9 lesions	50/73 (68.5%)	30/55 (54.5%)	47/91 (51.6%)	46/119 (38.7%)	11/20 (55.0%)	257/488 (52.7%)
10–100 lesions	19/73 (26.0%)	24/55 (43.6%)	40/91 (44.0%)	68/119 (57.1%)	9/20 (45.0%)	202/488 (41.4%)
> 100 lesions	0/73 (0%)	0/55 (0%)	4/91 (4.4%)	4/119 (3.4%)	0/20 (0%)	10/488 (2.0%)
Unknown	4/73 (5.5%)	1/55 (1.8%)	0/91 (0%)	1/119 (.8%)	0/20 (0%)	19/488 (3.9%)

Table S7. Longitudinal outcomes among patients with baseline, during, and posttreatment completion information (n=104 patients)[1]

Outcome	Baseline	Day 1 – 7	Day 8 – 14	Posttreatment
Approximate number of lesions, n	15	76	83	89
Median (IQR)	15.0 (10.5–28.0)	13.0 (5.0–25.0)	2.0 (0–8.5)	0 (0–0)
Percent body affected, n	78	76	79	84
Median (IQR)	5.0% (2.0–10.0%)	5.0% (1.0–10.5%)	1.0% (0–5.0%)	0% (0–0%)
New lesions developed after initiation of tecovirimat				
Yes	--	16 (15.4%)	7 (6.7%)	2 (1.9%)
No	--	72 (69.2%)	89 (85.6%)	96 (92.3%)
Unknown	--	16 (15.4%)	8 (7.7%)	6 (5.8%)
Strictures in genital area				
Yes	--	2 (2.0%)	4 (3.9%)	0 (0%)
No	--	73 (70.2%)	77 (74.0%)	0 (0%)
Unknown		29 (27.9%)	23 (22.1%)	104 (100%)
Evidence of scarring/depigmentation				
Yes	--	20 (19.2%)	29 (27.9%)	41 (39.4%)
No	--	59 (56.7%)	55 (52.9%)	49 (47.1%)
Unknown	--	25 (24.0%)	20 (19.2%)	14 (13.5%)
All lesions crusted and healed with new layer of skin				
Yes	--	12 (11.5%)	53 (51.0%)	74 (71.2%)
No	--	69 (66.4%)	34 (32.7%)	15 (14.4%)
Unknown	--	23 (22.1%)	17 (16.4%)	15 (14.4%)

[1] Data summarized of patients with baseline intake form and outcome form containing information on clinical progress during day 1–7 and day 8–14 treatment, and posttreatment completion. Among patients in this subset, 51 (49.0%) were white and 29 (27.9%) were black. A total of 20 (19.2%) of patients were Hispanic or Latino. Median age of patients was 37.0 years (IQR 31.0 – 45.8). Severely immunocompromised patients accounted for 4 (3.8%) of patients.

Table S8. Demographics and characteristics among patients with an intake form only (n=6,138) and patients with matching intake and outcome forms (n=1,043)[1]

	Patients with Intake Form Only (n=6,138)	Patients with Intake and Outcome Forms (n=1,043)
Sex assigned at birth — no. (%)		
Male	5,295 (86.3%)	1,005 (96.4%)
Female	181 (2.9%)	27 (2.6%)
Unknown	662 (10.8%)	11 (1.1%)
Gender identity — no. (%)		
Male	5,024 (81.9%)	745 (71.4%)
Female	171 (2.8%)	22 (2.1%)
Transgender female	103 (1.7%)	9 (0.9%)
Transgender male	29 (0.5%)	4 (0.4%)
Other	39 (0.6%)	5 (0.5%)
Unknown	772 (12.6%)	258 (24.7%)
Median age, years (IQR) — no. (%)	35.0 (30.0–43.0)	36.0 (31.0–42.0)
Age group — no. (%)		
< 6 months	3 (0.0%)	1 (0.1%)
6 months to < 12 months	2 (0.0%)	0 (0.0%)
1 to < 6 years	4 (0.1%)	3 (0.3%)
6 to < 12 years	2 (0.0%)	2 (0.2%)
12 to < 18 years	7 (0.1%)	5 (0.5%)
18 to < 65 years	5,964 (97.2%)	1,012 (97.0%)
≥ 65 years	51 (0.8%)	11 (1.1%)
Unknown	105 (1.7%)	9 (0.9%)
Ethnicity — no. (%)		
Hispanic or Latino	1,817 (29.6%)	264 (25.3%)

	Patients with Intake Form Only (n=6,138)	Patients with Intake and Outcome Forms (n=1,043)
Not Hispanic or Latino	3,370 (54.9%)	615 (59.0%)
Unknown	951 (15.5%)	164 (15.7%)
Race — no. (%)		
White	2,673 (43.5%)	517 (49.6%)
African American/Black	1,746 (28.4%)	244 (23.4%)
Asian	166 (2.7%)	25 (2.4%)
Other	760 (12.4%)	134 (12.8%)
Unknown	793 (12.9%)	123 (11.8%)
Hospitalized		
Inpatient	803 (13.1%)	131 (12.6%)
Outpatient	4,507 (73.4%)	900 (86.3%)
Unknown	828 (13.5%)	12 (1.2%)

1 Patients with an intake form only with no outcome form analyzed due to missing outcome form or outcome form with missing posttreatment completion information (n=6,138) compared to patients with matching intake and outcome forms (n=1,043).

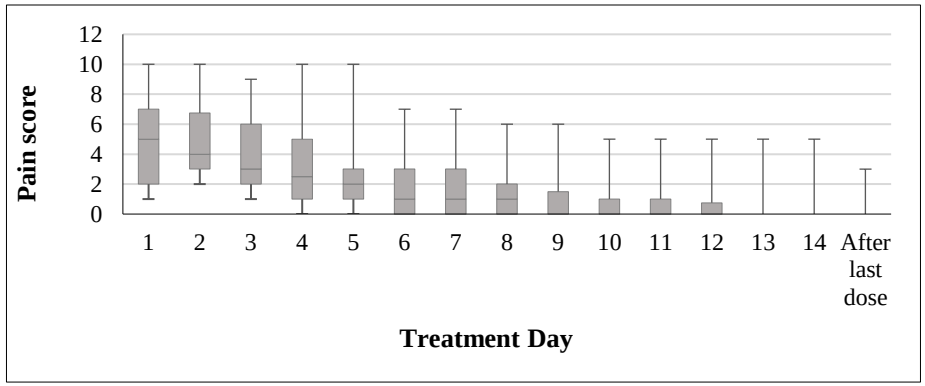

Figure S1. Pain score self-reported on patient diaries among patients treated with tecovirimat (n=91)
Figure summarizes pain score (from 0–10 where 10 was severe pain) among 91 patients with at least one pain score reported on any day during or after tecovirimat treatment.

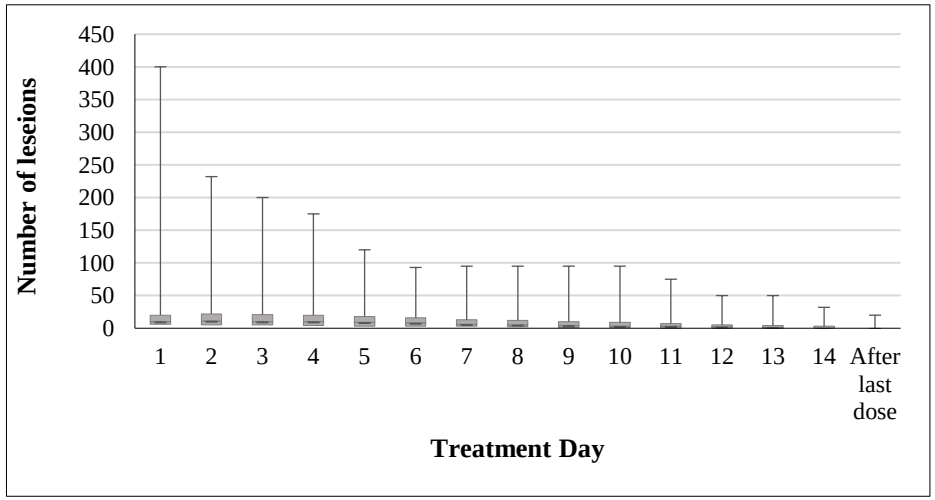

Figure S2. Approximate number of lesions self-reported on patient diaries among patients treated with tecovirimat (n=160)
Figure summarizes data among 160 patients with approximate number of lesions reported on at least one day during or after tecovirimat treatment.

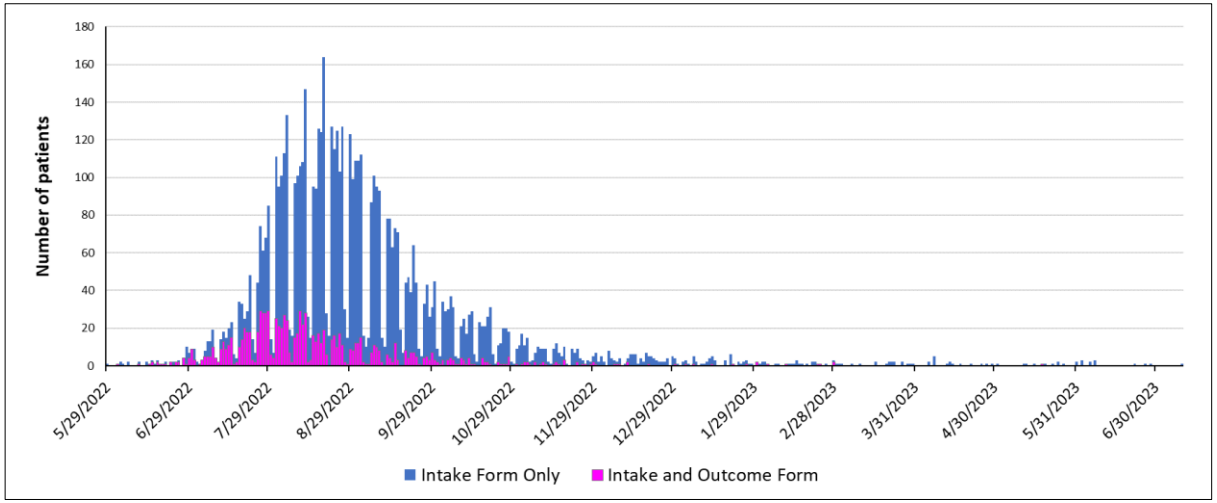

Figure S3. Number of patients by date among patients with an intake form only (n=6,138) and patients with matching intake and outcome forms (n=1,043)

Patients with an intake form only with no outcome form analyzed due to missing outcome form or outcome form with missing post-treatment completion information (n=6,138) compared to patients with matching intake and outcome forms (n=1,043).

Table S9. Reported serious adverse events from returned Clinical Outcome and MedWatch forms (223 serious adverse events among 132 patients)[1]

System Organ Class (Adverse Event)	Number of events
Blood and lymphatic system disorders	**4**
Eosinophilia	1
Hemolytic uremic syndrome	1
Leukocytosis	1
Thrombocytopenia	1
Cardiac disorders	**4**
Asystole	1
Cardiac arrest	1
Myocardial infarction	1
Palpitations	1
Death	**40**
Death	40
Eye disorders	**3**
Blurred vision	2
Periorbital edema	1
Gastrointestinal disorders	**35**
Abdominal pain	6
Diarrhea	4
Dyspepsia	1
Dysphagia	1
Mucositis ulcer	1
Nausea	10
Sore throat	1
Tooth discoloration	1
Vomiting	10
General disorders and administration site conditions	**22**
Edema	3
Fatigue	7
Fever	4
Flu-like symptoms	1
Localized edema	1
Malaise	1
Multi-organ failure	3
Non-cardiac chest pain	2
Hepatobiliary disorders	**9**
Elevated liver enzymes	8
Hepatic Failure	1
Immune system disorders	**4**
Allergic Reaction	1

System Organ Class (Adverse Event)	Number of events
Anaphylaxis	1
Immune System Disorders	1
Kaposi inflammatory cytokine syndrome	1
Infections and infestations	**9**
Appendicitis	1
Bacteremia	3
Cytomegalovirus infection reactivation	2
Sepsis	2
Skin infection	1
Laboratory abnormalities	**4**
Creatinine increased	2
Eosinophilia	1
Neutrophil count decreased	1
Metabolism and nutrition disorders	**2**
Anorexia	1
Hypokalemia	1
Musculoskeletal and connective tissue disorders	**3**
Arthralgia	1
Muscle weakness lower limb	1
Myalgia	1
Nervous system disorders	**31**
Dizziness	5
Headache	12
Paresthesia	3
Pruritis	1
Seizure	3
Stuttering	1
Syncope	1
Tremor	5
Psychiatric disorders	**7**
Depression	1
Hallucinations	3
Insomnia	1
Psychiatric disorders - Other, specify	1
Suicidal ideation	1
Renal and urinary disorders	**11**
Acute kidney injury	7
Dysuria	1
Hematuria	1
Urinary retention	2
Respiratory, thoracic and mediastinal disorders	**8**

System Organ Class (Adverse Event)	Number of events
Adult respiratory distress syndrome	2
Dyspnea	1
Hypoxia	1
Pleural effusion	1
Respiratory failure	2
Respiratory, thoracic and mediastinal disorders	1
Skin and subcutaneous tissue disorders	**24**
Dry skin	1
Finger discoloration	1
Hyperhidrosis	1
Paraphimosis	1
Pruritis	6
Rash maculopapular	1
Rash, unspecified	4
Soft tissue infection	1
Urticaria	8
Vascular disorders	**3**
Hypotension	2
Superficial thrombophlebitis	1

1 Serious adverse events (SAEs) and selected adverse events were required to be reported regardless of causality via the MedWatch form and clinical outcome form within 72 hours of treating clinician's awareness.

2 Elevated liver enzymes started to be observed as soon as 1 day after tecovirimat initiation. High alanine transaminase (ALT) and aspartate transaminase (AST) values in five patients with reported information ranged from 176–328 for ALT and 67–332 for AST.

Sample EA-IND Report Forms

Patient Intake Form

Treating physician or designee should complete this form to provide patient's baseline condition **prior** to tecovirimat initiation. Return to CDC within **3 working days** of initiation of therapy.

HOSPITAL INFORMATION

Treating Physician Name	**Telephone number**	**Email address**

Hospital/Medical Facility Name	**Date of assessment** (mm/dd/yy):

PATIENT INFORMATION

Patient Name (first and last name)	**Date of Birth**

Sex assigned at birth	**Gender patient identifies as**	**Pregnant**
☐ M ☐ F	☐ M ☐ F ☐ Transgender male ☐ Transgender female ☐ Other ☐ Unknown	☐ Yes ☐ No ☐ Unknown If yes, weeks of gestation:____ ☐ Unknown

Ethnicity	**Race** (check all that apply)	
☐ Hispanic or Latino	☐ African American/Black	☐ American Indian or Alaska Native
☐ Not Hispanic or Latino	☐ Asian	☐ Native Hawaiian or Other Pacific Islander
☐ Unknown	☐ White	☐ Other ☐ Unknown

Patient Cell Phone:	**Patient Email Address:**	Patient has been informed that contact information may be provided to CDC for potential follow-up surveys: ☐ Yes ☐ No ☐ Unknown Patient Diary Form given: ☐ Yes ☐ No ☐ Unknown

ELIGIBILITY CRITERIA for TECOVIRIMAT TREATMENT

1. Primary Treatment for Orthopoxvirus Infections

- Does the patient have laboratory confirmed orthopoxvirus infection? ☐ Yes ☐ No ☐ Unknown
- Has the orthopoxvirus species been confirmed ☐ Yes ☐ No ☐ Unknown
  If yes, indicate species:_____ ☐ Unknown
- Date of last exposure: _____ ☐ Unknown
- Reason for tecovirimat treatment:
  ☐ Risk of severe outcome due to immunosuppression ☐ Lesions in sensitive anatomical areas
  ☐ Pain ☐ Other, specify:_____

OR

2. Post-exposure prophylaxis for high-risk contact of a confirmed or probable orthopoxvirus positive case
☐ Yes ☐ No ** Note: PEP use is determined on an individual basis in consultation with CDC.**

Indicate orthopoxvirus species:_____
Date of last exposure: _____ ☐ Unknown

OR

3. Secondary Treatment for Complications Resulting from Vaccinia Vaccination/Exposure
3a. Has the patient developed vaccine-related complications from being vaccinated with vaccinia vaccine?
☐ Yes ☐ No
If Yes, Date of Vaccination: _____

OR

3b. Has the patient been exposed to vaccinia virus without vaccination and developed vaccinia-related complications? ☐ Yes ☐ No Date of last exposure: _____ ☐ Unknown

- What is the complication? (check one below)
  - ☐ Severe generalized vaccinia (GV),
    Describe the extent of lesions and other systemic manifestations of GV:
    _____
  - ☐ Eczema vaccinatum
  - ☐ Progressive vaccinia (vaccinia necrosum)
  - ☐ Serious inadvertent inoculation, describe how assessed and systemic findings:
    _____

INELIGIBILITY FOR TECOVIRIMAT TREATMENT

1. Unwilling to sign informed consent.	☐ Yes ☐ No
2. Refuse tecovirimat treatment.	☐ Yes ☐ No
3. Known allergy to tecovirimat and/or inactive ingredients of tecovirimat.	☐ Yes ☐ No ☐ Unknown
4. For IV tecovirimat only: patients with severe renal impairment (creatinine clearance <30 mL/min)	☐ Yes ☐ No ☐ N/A

MEDICAL HISTORY

Date of illness onset: ☐ Unknown	**Date of exposure**: ☐ Unknown
Patient started as inpatient or outpatient? ☐ Inpatient, date of admission: ☐ Outpatient	**Admitted to ICU?** ☐ Yes if yes, date: ☐ No

Does patient have history of prior smallpox vaccination? ☐ Yes ☐ No ☐ Unknown

- If yes, indicate the vaccine received: ☐ ACAM2000 ☐ Jynneos ☐ Unknown
- Date(s) of vaccination: _____ ☐ Unknown
- If vaccinated with ACAM2000, was there a documented vaccine "take"?
  ☐ Yes ☐ No If yes, date of take: _____

Medical History (may attach notes from medical record)

☐ HIV/AIDS

☐ Atopic dermatitis or eczema ☐ active ☐ historical

☐ Other skin disease, specify: _____ ☐ active ☐ historical

☐ Congenital/acquired immune defect

☐ Autoimmune/connective tissue disorder

☐ Bone marrow/organ transplant

☐ Leukemia

☐ Lymphoma

☐ Other infection(s); specify: _____

☐ Other cancer; specify: _____

☐ Other pre-existing condition(s); specify: _____

Vital signs (to the extent feasible to be collected)

Patient Weight (kg):	Height (ft. in.):	Pulse (bpm):	Temperature (°F):

SIGNS/SYMPTOMS ON INITIAL PRESENTATION

Number of lesions	**Size of maximal lesion** (mm)	**Percent of body affected** (%)	**Lesion photos taken?**
☐ < 10 lesions ☐ 10 – 100 lesions ☐ > 100 lesions Approximate #: _____			☐ Yes Date(s) taken: _____ If yes, send photos to CDC ☐ No

Clinical Narrative (*please describe presenting illness, signs and symptoms, including type, site and circumstances of exposure, and lesion characteristics; may attach electronic summary visit from patient's EHR*)

DISTRIBUTION OF LESIONS

Left				**Right**			
☐ Scalp	☐ Face	☐ Mouth	☐ Oral mucosa	☐ Scalp	☐ Face	☐ Mouth	☐ Oral mucosa
☐ Throat	☐ Eye	☐ Hand	☐ Arm	☐ Throat	☐ Eye	☐ Hand	☐ Arm
☐ Trunk	☐ Abdomen	☐ Buttock	☐ Genitals	☐ Trunk	☐ Abdomen	☐ Buttock	☐ Genitals
☐ Anus	☐ Thigh	☐ Calf	☐ Foot	☐ Anus	☐ Thigh	☐ Calf	☐ Foot
☐ Other, specify: _____				☐ Other, specify: _____			

LIST OF MEDICATIONS

(list all medications, especially any immunosuppressing medications and other antivirals or treatments for orthopoxvirus infection [tecovirimat can be used in conjunction with other therapies based on treating physician's clinical judgment]).
Note: Co-administration of tecovirimat with repaglinide may cause hypoglycemia. Monitor blood glucose and monitor for hypoglycemic symptoms during co-administration. Co-administration with midazolam may reduce concentration of midazolam; monitor effectiveness of midazolam in patients.

Medication	**Dosage/Frequency**	**Administration route**	**Dates of administration**
Tecovirimat		☐ Oral ☐ IV	☐ Date first dose taken **or** ☐ Date prescribed:

OPTIONAL CLINICAL LABORATORY TESTING

Attach a copy of clinical laboratory results (e.g., hematology, chemistry, urinalysis) if any were performed per treating physician's clinical judgment depending on a patient's underlying clinical conditions to monitor the safety of tecovirimat treatment as appropriate (i.e., baseline, during, post treatment).

Tecovirimat Clinical Outcome Form

Treating clinician or designee should complete this form during and after completion of the tecovirimat treatment course and return to CDC with 3 working days of last patient follow-up.

PATIENT INFORMATION

Patient Name (first and last name):

HOSPITAL INFORMATION

Hospital/Medical Facility Name

Name of individual completing this form	**Contact information (email address, telephone number)**

TECOVIRIMAT TREATMENT INFORMATION

Route	**Date of 1st dose**	**Dose (mg)**	**Dose frequency**	**Duration of therapy (days)**
Oral				
IV				

- Did patient report taking oral tecovirimat with a meal containing about 600 calories and 25 grams of fat?
  ☐ Yes ☐ No ☐ N/A ☐ Unknown
- Was oral tecovirimat given via nasogastric (NG) tube?
  ☐ Yes ☐ No ☐ N/A ☐ Unknown

Any serious adverse events* with tecovirimat treatment? ☐ Yes ☐ No ☐ Unknown

- If yes, describe the SAE:
- Was the SAE reported to FDA MedWatch? ☐ Yes ☐ No ☐ Unknown
- If No or Unknown, please email a completed PDF MedWatch Form to regaffairs@cdc.gov.

**SAE defined as death, life-threatening AE, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions; congenital anomaly/birth defect; an important medical event that based on appropriate medical judgement may jeopardize the patient and may require medical or surgical intervention to prevent one of the outcomes listed.*

CLINICAL OUTCOME

Was patient hospitalized after tecovirimat initiation? ☐ Yes ☐ No ☐ Unknown

- Reason for admission:_____
- Hospital duration (# days): _____

Admitted to ICU? ☐ Yes ☐ No ☐ Unknown

- Duration of intensive care (# days):_____

Time to first observed (including patient-reported) improvement

- Signs/symptoms first started to improve on tecovirimat treatment day # _____
- Describe the improvements:

What was the outcome of the patient?

☐ Recovered from orthopoxvirus infection without sequelae
☐ Recovered from orthopoxvirus infection with sequelae
Describe sequelae: _____
☐ Not recovered from orthopoxvirus infection (e.g., persistence of residual lesions)
Describe: _____
☐ Death If patient died, when did patient die (date)? _____
What was the cause of death? _____

ASSESSMENT OF LESIONS DURING AND AFTER TECOVIRIMAT TREATMENT

Conduct patient follow-up once during treatment **(A or B)** and 7-10 days post treatment **(C)**. Day on which post-treatment follow-up is conducted is flexible (indicate date of assessment and findings on that day). Patient follow-ups may be conducted via **telemedicine.**

	During Tecovirimat Treatment		**After Completion of Tecovirimat Course**	
	Day 1-7 (A)	**Day 8-14 (B)**	**7-10 days after last tecovirimat dose (C)**	**Upon discharge (for inpatients only)**
Date of assessment				
Tecovirimat treatment day # *or* # days after last tecovirimat dose				
Approximate # of lesions				
% of body affected				
Size of maximal lesion (mm)				
Any new lesions? *If yes, send new lesion samples to CDC for resistance testing,* ***if feasible***	☐ Yes ☐ No Date of new lesions:	☐ Yes ☐ No Date of new lesions:	☐ Yes ☐ No Date of new lesions:	☐ Yes ☐ No Date of new lesions:
All lesions crusted and healed with new layer of skin?	☐ Yes ☐ No Describe:	☐ Yes ☐ No Describe:	☐ Yes ☐ No Describe:	☐ Yes ☐ No Describe:
Evidence of scarring or depigmentation?	☐ Yes ☐ No Describe:	☐ Yes ☐ No Describe:	☐ Yes ☐ No Describe:	☐ Yes ☐ No Describe:
Strictures in the genital region?	☐ Yes ☐ No Describe:	☐ Yes ☐ No Describe:	☐ Yes ☐ No Describe:	☐ Yes ☐ No Describe:

Describe the anatomical locations of the lesions and how the lesions changed throughout the treatment course (e.g., size, location, rate of healing). *If any photos of lesions were taken, please include with the dates the photos were taken.*

<u>OPTIONAL</u> CLINICAL LABORATORY TESTING

Attach a copy of clinical laboratory results (e.g., hematology, chemistry, urinalysis) if any were performed per treating physician's clinical judgment depending on the patient's underlying clinical conditions to monitor the safety of tecovirimat treatment as appropriate (e.g., baseline, during, post treatment).

OPTIONAL: LESION/SCAB* SAMPLING FOR RESISTANCE TESTING AT CDC **Complete this section only if any samples were collected and shipped to CDC**			
Were samples collected & sent to CDC? ☐ Yes ☐ No			
Sample type	**Anatomical location of lesion**	**Date of sample collection**	**Date sample sent to CDC**

* Samples of any new lesions that developed during tecovirimat treatment and after treatment completion to CDC for resistance testing.

OPTIONAL: PLASMA PHARMACOKINETIC (PK) SAMPLING **Complete this section only if any samples were collected and shipped to Alturas**		
Date and Time of PK Sample Collection	**Date and Time of Tecovirimat Dose**	**Tecovirimat Dose (oral, NG tube, or IV) on PK collection** **Dose taken with meal?**
____/_____/_____ ____:____	____/_____/_____ ____:____	☐ Oral ☐ NG Tube ☐ IV
____/_____/_____ ____:____	____/_____/_____ ____:____	☐ Oral ☐ NG Tube ☐ IV

Patient Diary - Tecovirimat Capsules

Instructions for Patients: Remember to take tecovirimat capsules with **a full glass of water** and after eating a **full, fatty meal** (containing about 600 calories and 25 grams of fat). It is important to report any side effects (symptoms you experience) with tecovirimat. Please use this form to record how you feel and any side effects to tecovirimat.

Patient first and last name:	**Date of birth** (mm/dd/yyyy):
Cellphone number:	**Email address:**
Date of first tecovirimat dose (mm/dd/yy):	**Date of last tecovirimat dose** (mm/dd/yy):
Did you take each dose of tecovirimat with a full, fatty meal? ☐ Yes ☐ No ☐ Don't know	

Progress	**Record Every Day While Taking Tecovirimat**														**After Tecovirimat**
	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14	7 days after your last dose
Approximate # of lesions															
Any new lesions? (Y/N – if Y, describe on next page)															
Are lesions improving? (Y/N)															
Any pain with lesions? (enter a #) **0:** No pain **1-3**: Mild pain **4-6**: Moderate pain **7-9**: Severe pain **10**: Most severe pain															
Compared to the previous day, are you generally feeling: (enter a #) **1**: Much worse **2**: Worse **3**: About the same **4**: A little better **5**: Much better															

Comments on progress (such as any new or no new lesions, healed lesions)

Side Effects to Tecovirimat: Please indicate whether you experienced any of the following side effects during tecovirimat therapy.		
Nausea ☐ Yes ☐ No	Abdominal Pain ☐ Yes ☐ No	Red or purple spots on the skin ☐ Yes ☐ No
Vomiting ☐ Yes ☐ No	Bruising ☐ Yes ☐ No	Pins and needles sensation ☐ Yes ☐ No
If diabetic and taking repaglinide, experienced low sugar levels? (e.g., shakiness, sweating, hunger, lightheadedness) ☐ Yes ☐ No	Fainting ☐ Yes ☐ No	Seizure ☐ Yes ☐ No
Other, describe:		

List all other medications you were taking while on tecovirimat		
Name of medication	**Dose**	**Dates taken**