Drug-Drug Interactions Between Antiretroviral Medications and Medications for Treatment of Severe Mpox

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(also see drug package inserts and CDC Treatment Information for Healthcare Professionals)

→ *Tecovirimat, vaccinia immune globulin intravenous (VIGIV), cidofovir, brincidofovir*

ARV or Class	Mechanism of Action	Clinical Comments
All NRTIs (ABC, TDF, TAF,3TC, FTC)	**Cidofovir:** Eliminated via glomerular filtration and active renal secretion by OAT1, OAT3	• **Cidofovir:** Avoid coadministration with nephrotoxic agents. Consider use of TAF in place of TDF and monitor for renal adverse events • **Brincidofovir, tecovirimat, VIGIV:** Drug interactions unlikely
All NNRTIs (DOR, RPV [a], EFV, ETR)	**Tecovirimat:** Weak inducer of CYP3A and weak inhibitor of CYP2C8, CYP2C19; may potentially increase or decrease plasma concentrations of other medications	• **Tecovirimat:** Potential reduction in NNRTI levels, though effects not likely to be clinically relevant. No dose adjustment in either drug is necessary • **Brincidofovir, cidofovir, VIGIV:** Drug interactions unlikely
All PIs (ATV, DRV)	• **Brincidofovir:** Substrate for OATP1B1, OATP1B3 • **Tecovirimat:** Weak inducer of CYP3A and weak inhibitor of CYP2C8, CYP2C19	• **Brincidofovir:** Coadministration with PIs will likely increase brincidofovir levels. Consider avoiding concurrent PIs if possible. If unable to change PI, monitor for brincidofovir-related adverse events, which include LFT elevations, hyperbilirubinemia, diarrhea, or other GI adverse events. Postpone PI dosing for at least 3 hours AFTER brincidofovir administration • **Tecovirimat:** Potential reduction in PI levels, though effects not likely to be clinically relevant. No dose adjustment in either drug is necessary • **Cidofovir, VIGIV:** Drug interactions unlikely
BIC, CAB IM or oral, DTG, RAL	No clinically significant interactions	No dose adjustments necessary
EVG, boosted	• **Brincidofovir:** Substrate for OATP1B1, OATP1B3 • **Tecovirimat:** Weak inducer of CYP3A and weak inhibitor of CYP2C8, CYP2C19	• **Brincidofovir:** Coadministration with EVG/COBI will likely increase brincidofovir levels. Consider avoiding concurrent EVG/COBI if possible. If unable to change EVG/COBI, monitor for brincidofovir-related adverse events, which include LFT elevations, hyperbilirubinemia, diarrhea, or other GI adverse events. Postpone EVG/COBI dosing for at least 3 hours AFTER brincidofovir administration • **Tecovirimat:** Potential reduction in EVG/COBI levels, though effects not likely to be clinically relevant. No dose adjustment in either drug is necessary
FTR	• **Brincidofovir:** Substrate for OATP1B1, OATP1B3 • **Tecovirimat:** Weak inducer of CYP3A and weak inhibitor of CYP2C8, CYP2C19	• **Brincidofovir:** FTR inhibits OATP1B1 and may increase brincidofovir levels. Avoid concurrent use if possible. If unable to change therapy, monitor for brincidofovir-related adverse events, which include LFT elevations, hyperbilirubinemia, diarrhea, or other GI adverse events. Postpone FTR dosing for at least 3 hours AFTER brincidofovir administration • **Tecovirimat:** Potential reduction in FTR levels, though effects not likely to be clinically relevant. No dose adjustment in either drug is necessary
MVC [a]	**Tecovirimat:** Weak inducer of CYP3A and weak inhibitor of CYP2C8, CYP2C19	**Tecovirimat:** Potential reduction in MVC levels, though effects not likely to be clinically relevant. No dose adjustment in either drug is necessary

Abbreviations: 3TC, lamivudine; ABC, abacavir; ARV, antiretroviral; ATV, atazanavir; AUC, area under the curve; BIC, bictegravir; CAB, cabotegravir; COBI, cobicistat; CYP, cytochrome P450; DOR, doravirine; DRV, darunavir; DTG, dolutegravir; EFV, efavirenz; ETR, etravirine; EVG, elvitegravir; FTC, emtricitabine; FTR, fostemsavir; GI, gastrointestinal; IM, intramuscular; LFT, liver function test; MVC, maraviroc; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; OAT, organic anion transporter; OATP, organic anion transporting polypeptide; PI, protease inhibitor; RAL, raltegravir; RPV, rilpivirine; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; VIGIV, vaccinia immune globulin intravenous.

Note:

a. No data is currently available on effects related to concurrent use of tecovirimat and HIV medications. However, midazolam AUC was reduced by 32% with concomitant tecovirimat use, and some experts recommend caution due to the mild CYP3A4 induction associated with tecovirimat. Among them is University of Liverpool HIV Drug Interactions, which makes the following dosing change recommendations, although they are not based on any clinical data:
-RPV: Increase dose to 50 mg daily for the duration of tecovirimat treatment and for 2 weeks after tecovirimat is stopped.
-MVC: Increase dose to 600 mg twice daily (if the patient is not taking another potent CYP3A4 inhibitor concurrently) for the duration of tecovirimat treatment and for 2 weeks after tecovirimat is stopped. If the patient is receiving concomitant treatment with a potent CYP3A4 inhibitor, MVC should be dosed at 150 mg twice daily for the duration of concurrent tecovirimat.
-DOR: Increase dose to 100 mg twice daily for the duration of tecovirimat treatment and for 2 weeks after tecovirimat is stopped.