Resource: ART Drug-Drug Interactions

August 2024

Table 47: Mpox Treatments (also see drug package inserts and CDC: Mpox Treatment Information for Healthcare Professionals)		
→ Tecovirimat [a], vaccinia immune globulin intravenous (VIGIV), cidofovir, brincidofovir		
Class or Drug	**Mechanism of Action**	**Clinical Comments**
• Bictegravir (BIC) • Cabotegravir (CAB), IM or oral • Dolutegravir (DTG) • Raltegravir (RAL)	No clinically significant interactions expected.	No dose adjustments are necessary.
All NRTIs	**Cidofovir** is eliminated via glomerular filtration and active renal secretion by OAT1 and OAT3.	• **Cidofovir:** Avoid coadministration with nephrotoxic agents. Consider use of TAF in place of TDF and monitor for renal-related adverse effects. • **Brincidofovir, tecovirimat, VIGIV:** Drug interactions are unlikely.
All NNRTIs	**Tecovirimat** is a weak inducer of CYP3A and a weak inhibitor of CYP2C8 and CYP2C19; use may potentially increase or decrease plasma concentrations of other medications.	• **Tecovirimat** may reduce NNRTI levels, though effects are not likely to be clinically relevant. No dose adjustment in either drug is necessary. • **Brincidofovir, cidofovir, VIGIV:** Drug interactions are unlikely.
All PIs	• **Brincidofovir** is a substrate for OATP1B1 and OATP1B3. • **Tecovirimat** is a weak inducer of CYP3A and weak inhibitor of CYP2C8 and 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 effects, e.g., LFT elevations, hyperbilirubinemia, diarrhea, or other GI adverse effects. Postpone PI dosing for at least 3 hours *after* brincidofovir administration. • **Tecovirimat** may reduce PI levels, though effects are not likely to be clinically relevant. No dose adjustment in either drug is necessary. • **Cidofovir, VIGIV:** Drug interactions are unlikely.
Elvitegravir (EVG), boosted	• **Brincidofovir** is a substrate for OATP1B1 and OATP1B3. • **Tecovirimat** is weak inducer of CYP3A and weak inhibitor of CYP2C8 and 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 effects, e.g., LFT elevations, hyperbilirubinemia, diarrhea, or other GI adverse effects. Postpone EVG/COBI dosing for at least 3 hours *after* brincidofovir administration. • **Tecovirimat** may reduce EVG/COBI levels, though effects are not likely to be clinically relevant. No dose adjustment in either drug is necessary.

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Class or Drug	Mechanism of Action	Clinical Comments
Fostemsavir (FTR)	• **Brincidofovir** is a substrate for OATP1B1 and OATP1B3. • **Tecovirimat** is a weak inducer of CYP3A and a weak inhibitor of CYP2C8 and 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 effects, e.g., LFT elevations, hyperbilirubinemia, diarrhea, or other GI adverse effects. Postpone FTR dosing for at least 3 hours *after* brincidofovir administration. • **Tecovirimat** may reduce FTR levels, though effects are not likely to be clinically relevant. No dose adjustment in either drug is necessary.
Maraviroc (MVC)	**Tecovirimat** is a weak inducer of CYP3A and a weak inhibitor of CYP2C8 and CYP2C19.	**Tecovirimat** may reduce MVC levels, though effects are not likely to be clinically relevant. No dose adjustment in either drug is necessary.

Abbreviations: ARV, antiretroviral; AUC, area under the curve; CDC, Centers for Disease Control and Prevention; COBI, cobicistat; CYP, cytochrome P450; GI, gastrointestinal; IM, intramuscular; LFT, liver function test; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; OAT, organic anion transporter; OATP, organic anion transporting polypeptide; PI, protease inhibitor.

Note:

a. No data are 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.