ANTI-INFECTIVES:
AZOLE ANTIFUNGALS AND MACROLIDES

	INSTIs		NNRTIs			PIs
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)*	• ETRAVIRINE *(Intelence)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • NEVIRAPINE *(Viramune)*	Boosted with ritonavir (Norvir) or cobicistat • ATAZANAVIR *(Reyataz, Evotaz)* • DARUNAVIR *(Prezista, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*
AZOLE ANTIFUNGALS						
• Fluconazole *(Diflucan)*		Potential for ↑ azole		Potential for ↑ NNRTI and ↓ azole. Monitor for toxicity and antifungal efficacy.	Efavirenz Potential for ↑ nevirapine; monitor for toxicity.	
• Itraconazole *(Sporanox)*		Potential for ↑ azole. Use maximum 200 mg itraconazole per day.		Potential for ↑ NNRTI and ↓ azole. Monitor for toxicity and antifungal efficacy.	Potential for ↓ azole	Potential for ↑ azole. Use maximum 200 mg itraconazole per day.
• Ketoconazole *(Nizoral)*		Potential for ↑ azole. Use maximum 200 mg ketoconazole per day.		Potential for ↑ NNRTI and ↓ azole. Monitor for toxicity and antifungal efficacy.	Potential for ↓ azole	Potential for ↑ azole. Use maximum 200 mg ketoconazole per day.
• Posaconazole *(Posanol)*		Potential for ↑ azole		Potential for ↑ NNRTI and ↓ azole. Monitor for toxicity and antifungal efficacy.	Efavirenz: potential for ↓ azole Potential for ↑ nevirapine; monitor for toxicity.	Potential for ↑ PI concentrations. Monitor for toxicity.

	INSTIs		NNRTIs			PIs
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)*	• ETRAVIRINE *(Intelence)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • NEVIRAPINE *(Viramune)*	Boosted with ritonavir (Norvir) or cobicistat • ATAZANAVIR *(Reyataz, Evotaz)* • DARUNAVIR *(Prezista, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*
• Voriconazole *(Vfend)*		Potential for ↑ azole		Potential for ↑ NNRTI and ↓ azole. Monitor for toxicity and antifungal efficacy.	Efavirenz: potential for ↓ voriconazole and ↑ efavirenz. Potential for ↓ azole	Potential for ↑/↓ voriconazole concentrations.
MACROLIDES						
• Azithromycin *(Zithromax)*						
• Clarithromycin *(Biaxin)*		↑ clarithromycin. Adjust dose with renal impairment.		Etravirine: Potential for ↓ clarithromycin and ↑ 14-OH metabolite and increased risk of rash.	Potential for ↑ rilpivirine, potential QT prolonga-tion	Potential for ↓ clarithromycin and ↑ 14-OH metabolite and increased risk of rash.	↑ clarithromycin. Adjust dose with renal impairment.
• Erythromycin							

Mechanism of Drug Interactions, Management and Monitoring

Azole Agent	Mechanism of Interaction	Main Interacting ARVs	Management	Monitoring
Fluconazole	Inhibition of CYP3A4	Doravirine, rilpivirine, etravirine, nevirapine, elvitegravir/cobicistat	Use standard doses of both drugs.	Antiretroviral toxicity
Itraconazole, ketoconazole, posaconazole	Inhibition of CYP3A4 (antiretrovirals)	Ritonavir and cobicistat-boosted PIs, elvitegravir/cobicistat	Use maximum 200 mg ketoconazole or itraconazole daily	Azole toxicity
	Substrate of CYP3A4, induction by most NNRTIs	Efavirenz, etravirine, nevirapine	Avoid efavirenz and nevirapine if possible. Use etravirine with caution and consider increasing azole dose if necessary.	Azole efficacy
Voriconazole	Induction of CYP2C19 by some antiretrovirals; voriconazole also inhibits CYP3A4.	Ritonavir-boosted PIs, efavirenz	Ritonavir-boosted PIs: avoid coadministration. Efavirenz: increase voriconazole to 400 mg q12hours and decrease efavirenz to 300 mg daily if therapy lasts more than few days.	Voriconazole efficacy.
	Inhibition of CYP2C19	Etravirine		Etravirine toxicity
	Inhibition of CYP3A4 (antiretrovirals and voriconazole)	Cobicistat-boosted PIs and elvitegravir/cobicistat		Voriconazole toxicity
Azithromycin	Substrate of CYP3A4 (minor)	Ritonavir- and cobicistat-boosted PIs and elvitegravir/cobicistat	Use standard doses of both drugs	Monitor for QT interval prolongation in patients with other pre-existing risk factors

Azole Agent	Mechanism of Interaction	Main Interacting ARVs	Management	Monitoring
Clarithromycin	Inhibition of CYP3A4 (ritonavir, cobicistat) Protease inhibitors inhibit the metabolism of clarithromycin via CYP3A4 and increase concentrations of clarithromycin. This may lead to a decrease in CLA-14 OH metabolite, reducing antibacterial activity versus gram-negative organisms.	Elvitegravir/cobicistat and boosted protease inhibitors	Atazanavir: reduce clarithromycin dose by 50% to avoid QTc prolongation and consider alternate agent for non-MAC infections. Elvitegravir/cobicistat: Reduce dose of clarithromycin by 50% if CrCl is between 50-60mL/min. Do not administer clarithromycin if CrCl <50mL/min. Darunavir and lopinavir: reduce clarithromycin dose by 50% if CrCl 30-60mL/min; by 75% if CrCl <30mL/min.	Monitor patients for signs of clarithromycin toxicity including QT interval prolongation
	Induction of CYP3A4 resulting in decreased clarithromycin and increased CLA-14 OH metabolite, which has reduced activity against Mycobacterium avium complex (MAC)	Efavirenz, etravirine, nevirapine	May wish to consider switching to azithromycin, particularly if treating MAC infection or consider non-interaction NNRTI such as doravirine.	Clarithromycin efficacy and potential rash
Clarithromycin, erythromycin	Inhibition of CYP3A4 (clarithromycin, erythromycin)	Rilpivirine	Use with caution.	Monitor for QT interval prolongation in patients with other pre-existing risk factors

Legend:

No dose adjustment required.

Use combination with caution. Adjustment in drug dose or frequency or additional/more frequent monitoring may be required. May wish to consult with a pharmacist knowledgeable in HIV drug interactions.

Contraindicated/avoid combination.

A MANAGEMENT TOOL FOR HIV DRUG-DRUG INTERACTIONS

Printed with the assistance of an unrestricted educational grant from:

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