OVER-THE-COUNTER, COMPLEMENTARY AND ALTERNATIVE AGENTS

VITAMINS AND MINERALS, HERBAL PRODUCTS, APPEARANCE AND PERFORMANCE ENHANCING SUPPLEMENTS

	INSTIs		NNRTIs		PIs	RTI	
	• BICTEGRAVIR *(Biktarvy)* • DOLUTEGRAVIR *(Tivicay, Triumeq, Juluca)* • RALTEGRAVIR *(Isentress)*	• ELVITEGRAVIR/ COBICISTAT *(Stribild, Genvoya)*	• DORAVIRINE *(Pifeltro, Delstrigo)* • RILPIVIRINE *(Edurant, Complera, Odefsey, Juluca)*	• EFAVIRENZ *(Sustiva, Atripla)* • ETRAVIRINE *(Intelence)* • NEVIRAPINE *(Viramune)*	• ATAZANAVIR *(Reyataz/Norvir, Evotaz)* • DARUNAVIR *(Prezista/Norvir, Prezcobix, Symtuza)* • LOPINAVIR *(Kaletra)*	• TENOFOVIR ALAFENAMIDE, TAF *(Descovy, Biktarvy, Genvoya, Odefsey, Symtuza)*	• TENOFOVIR DISOPROXIL, TDF *(Viread,Truvada, Atripla, Complera, Delstrigo, Stribild)* •ABACAVIR *(Kivexa, Ziagen, Triumeq)*
VITAMINS AND MINERALS							
• Vitamin D				Potential for ↓ vitamin D			
• Cations such as calcium, magnesium, iron, aluminum, zinc, including supplements and multivitamins with high dose calcium, iron	↓ INSTI Raltegravir 600 mg HD tablets Raltegravir 400 mg OK with calcium	Potential for ↓ INSTI					
HERBAL PRODUCTS AND SUPPLEMENTS							
• Echinacea	Potential ↓ bictegravir Dolutegravir, raltegravir		Potential for ↓ NNRTI				

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• Garlic	Potential for ↓ INSTI	Potential for ↓ INSTI	Potential for ↓ NNRTI	Potential for ↓ NNRTI	Potential for ↓ PI	Potential for ↓ TAF	
• Ginko biloba	Potential ↓ bictegravir Dolutegravir, raltegravir		Potential for ↓ NNRTI	Potential for ↓ NNRTI	Always use boosted PI		
• Grapefruit juice			Potential for ↑ rilpivirine				
• Milk thistle • Saw palmetto							

APPEARANCE AND PERFORMANCE ENHANCING SUPPLEMENTS (APES)

• Creatine	Potential additive ↑ Scr without impacting renal function	Potential additive ↑ Scr without impacting renal function	Rilpivirine: potential additive ↑ Scr without impacting renal function		Cobicistat-boosted PIs: potential additive ↑ Scr without impacting renal function		Tenofovir DF: Potential additive nephrotoxicity (rare)
• Testosterone (oral IM, topical)		Potential for ↑ testosterone		Potential for ↓ testosterone	Potential for ↑ testosterone		

	INSTIs		NNRTIs		PIs	RTI	
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Anabolic steroids • Oral: oxandrolone, stanozolol • IM: nandrolone							
Selective androgen receptor modulators • Andarine, ostarine							
Selective estrogen receptor modulators (SERMS) • Clomiphene, tamoxifen	Potential for tamoxifen to ↓ bictegravir	Potential for ↑ tamoxifen, possibly ↓ elvitegravir Clomiphene OK	Potential for ↓ NNRTI Clomiphene OK	Potential for ↓ tamoxifen and possibly ↓ NNRTI Clomiphene OK	Potential for ↑ tamoxifen, possibly ↓ PI Clomiphene OK		
Aromatase inhibitors • Letrozole, anastrazole		Potential for ↑ aromatase inhibitor		Potential for ↓ aromatase inhibitor	Cobicistat-boosted PI: Potential for ↑ aromatase inhibitor Ritonavir-boosted PI: potential for ↑/↓ aromatase inhibitor		

Mechanism of Drug Interactions, Management and Monitoring

Class	Mechanism of interaction	Main interacting ARVs	Management	Monitoring
Cation-containing products, including supplements and multivitamins	Chelation and decreased absorption Many Multivitamins including once daily and especially those designed for women with extra Calcium and iron, and those used during pregnancy, contain enough cations to lead to chelation of the integrase inhibitors and limit their absorption. This results in lowered levels of the integrase inhibitor and could result in loss of virologic suppression.	All INSTIs	Most multivitamin and supplement interactions can be managed by taking the integrase inhibitor simultaneously with food. Management recommendations vary according to specific INSTI: • **Bictegravir:** Administer bictegravir and polyvalent cations simultaneously with food, or separate by 2 hours. • **Dolutegravir:** Administer dolutegravir and polyvalent cations simultaneously with food, or take dolutegravir 2 hours before or 6 hours after polyvalent cations. • **Elvitegravir/c :** Stagger administration by at least 2 hours from mineral supplements. • **Raltegravir:** ONLY 400 MG BID dose may be used with calcium carbonate; use with other polyvalent cations is not recommended. Do not use 600 mg HD tablet with any polyvalent cations.	In all cases, monitor for continued viral suppression.
Echinacea	May induce CYP3A4 (mild)	Bictegravir, doravirine, rilpivirine	Potential for decreased ARV concentrations, clinical significance unclear.	Antiretroviral efficacy.

Class	Mechanism of interaction	Main interacting ARVs	Management	Monitoring
Garlic	May induce CYP3A4, Pgp	All ARVs	Avoid ingestion of large amounts of garlic (fresh, cooked or supplements)	Antiretroviral efficacy.
Gingko Biloba	Gingko may induce CYP3A4	bictegravir, unboosted atazanavir, NNRTIs,	Do not use unboosted atazanavir with Gingko. Consider elvitegravir/cobicistat, dolutegravir or raltegravir instead of bictegravir. Avoid Gingko with NNRTI; switch to boosted INSTI or INSTI metabolized via UGT, or boosted PI.	Antiretroviral efficacy.
Grapefruit juice	May inhibit CYP3A4, Pgp	rilpivirine	Clinical significance unclear; caution may be warranted if patient is on other drugs which inhibit CYP3A4 and/or have QT-prolonging effect	
Creatine	Creatine is metabolized to creatinine, and may lead to higher serum creatinine without necessarily impacting renal function. Potential additive effect when combined with ARVs which inhibit renal tubular secretion of creatinine.	Cobicistat, dolutegravir, bictegravir, rilpvirine	Increases in serum creatinine secondary to inhibition of renal tubular transporters generally occur soon after starting these antiretrovirals and remain stable thereafter. Use of creatine supplements may enhance this effect. If additional significant increases in serum creatinine occur after patient is stable on antiretrovirals, explore other causes of potential nephrotoxicity.	Monitor renal function.
	Potential additive risk of renal toxicity.	Tenofovir disoproxil	Some cases of renal impairment after use of creatinine have been reported.	Monitor renal function.
Aromatase inhibitors (anastrozole, letrozole)	Anastrazole: substrate of CYP3A4, UGT Letrozole: substrate of CYP3A4, 2A6	Protease inhibitors, elvitegravir/cobicistat (inhibition of CYP3A4, ritonavir may induce	Potential for increased or decreased concentrations of aromatase inhibitors.	Monitor for efficacy, toxicity of aromatase inhibitors.

Class	Mechanism of interaction	Main interacting ARVs	Management	Monitoring
		UGT), NNRTIs (induction of CYP3A4)		
Selective estrogen receptor modulators	Clomiphene: no metabolism/transporter effects. Tamoxifen: substrate and inducer of CYP3A4 Potential for increased tamoxifen with boosted regimens or decreased tamoxifen with enzyme inducing NNRTIs. Potential for decreased ARV concentrations via CYP3A4 induction by tamoxifen.	Bictegravir, elvitegravir/cobicistat, PIs, NNRTIs	Less interaction potential with clomiphene versus tamoxifen. If using tamoxifen, consider using an unboosted integrase inhibitor with minimal CYP3A4 involvement such as dolutegravir or raltegravir.	Efficacy/toxicity of tamoxifen. Antiretroviral efficacy.

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

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