ART Drug-Drug Interactions

Updated February 2021

Table 11: Etravirine (ETR) Interactions (also see drug package inserts)

Class or Drug	Mechanism of Action	Clinical Comments
Aliskiren	ETR is a minor inhibitor of P-gP and may minimally increase concentrations of aliskiren, but this has not been studied.	• When using with ETR, monitor for aliskiren-related adverse events. • If present, switch to alternative antihypertensive agent or ARV agent.
Warfarin	Could potentially increase (or more rarely decrease) metabolism of warfarin.	• Use cautiously with warfarin, and if use is necessary, increase monitoring of INR. • Increase dose slowly if INR decreases. Decrease dose if INR increases.
Antiplatelet drugs [Rathbun and Liedtke 2010; Kakuda, et al. 2011]	• **Cilostazol:** May reduce concentrations of cilostazol. • **Dipyridamole:** ETR may induce UGT enzymes, which are responsible for metabolism. • **Ticagrelor, clopidogrel:** ETR reduces ticagrelor concentrations and the conversion of clopidogrel to its active metabolite because ETR inhibits 2C19.	• **Cilostazol:** Monitor for antiplatelet effect; may be necessary to use an alternative antiplatelet drug or alternative ARV agent. • **Dipyridamole:** Monitor for antiplatelet effect; use another ARV agent if necessary. • **Ticagrelor, clopidogrel:** Use with ETR may reduce the antiplatelet effect; monitor closely and use an alternative ARV agent if possible.
Statins	• **Simvastatin, lovastatin:** Could potentially decrease concentrations. • Atorvastatin, pravastatin, fluvastatin: May modestly reduce concentrations.	• **Simvastatin, lovastatin:** Monitor for efficacy. May warrant increases in statin dose. Do not increase dose above maximum recommended statin dose. • **Atorvastatin, pravastatin, fluvastatin:** Monitor cholesterol-lowering effect of statins. May require increased dose.
Saxagliptin, sitagliptin	ETR may decrease concentration.	Monitor for efficacy; if necessary, increase dose of the DPP-4 inhibitor.
Inhaled and injected corticosteroids	Coadministration may reduce concentrations of corticosteroids.	**Systemic dexamethasone:** Consider alternative corticosteroid for long-term use; if benefits of use outweigh risks, monitor virologic response.
Trazodone	May decrease trazodone concentrations.	Monitor antidepressant and/or sedative effects.
Bupropion	No significant interactions.	Monitor clinical effect and increase as needed, but do not exceed recommended maximum dose.

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Alprazolam	Potential for reduced alprazolam concentrations.	Monitor for benzodiazepine withdrawal.
Diazepam	Potential for reduced diazepam concentrations.	No dose adjustments necessary.
Sleep medications	**Zolpidem:** Potential for reduced concentrations of zolpidem.	• **Zolpidem, eszopiclone:** Monitor for efficacy; no dose adjustments recommended. • **Suvorexant:** Monitor for efficacy; do not exceed 20 mg per day.
Antipsychotics	• **Aripiprazole, brexpiprazole:** Concentrations of aripiprazole and brexpiprazole may be decreased. • **Risperidone:** May decrease efficacy of risperidone.	• **Aripiprazole, brexpiprazole:** Monitor for efficacy; titrate dose slowly as needed; monitor for adverse effects. • **Risperidone:** Monitor for efficacy; titrate slowly; monitor for adverse effects.
Carbamazepine, oxcarbazepine, phenobarbital, phenytoin	Coadministration may significantly reduce concentrations of ARV agents through induction of CYP450 system.	• Coadministration is not recommended; use alternative anticonvulsant. • If benefit of use outweighs risk, monitor carefully for efficacy and toxicity. • Perform therapeutic drug monitoring if use cannot be avoided.
Lamotrigine, zonisamide	May reduce efficacy of lamotrigine or zonisamide.	Monitor efficacy; titrate dose slowly as needed.
Hormonal contraceptives	Information is based on what is known with EFV drug interactions.	• **Etonogestrel:** No data; consider alternative or additional contraceptive method or alternative ARV agent. • **Ulipristal:** Efficacy may be reduced; monitor closely.
Erectile and sexual dysfunction agents	• **PDE5 inhibitor:** Potential for reduced effectiveness of PDE5 inhibitors (sildenafil, vardenafil, and tadalafil). • **Flibanserin:** Potential for reduced concentrations of flibanserin.	• **PDE5 inhibitors:** Monitor clinical effect; if dose increase is needed to achieve desired clinical effect, titrate under medical supervision to lowest effective dose. • **Flibanserin:** Do not coadminister.
Bupropion	No significant interactions noted.	Monitor clinical effect and increase as needed, but do not exceed recommended maximum dose.
Buprenorphine	No significant interactions expected.	Monitor for signs of withdrawal or opioid toxicity and titrate dose of opioid or antagonist as required.

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Methadone	May slightly increase concentrations of methadone.	• Monitor for signs of withdrawal or opioid toxicity and titrate dose of opioid or antagonist as required. • Monitor for signs of methadone toxicity and reduce dose if necessary.
Cyclosporine, tacrolimus	Concentrations may be lower when used with ETR.	• Dose-adjust cyclosporine and tacrolimus based on efficacy and therapeutic drug monitoring (TDM). • Conduct TDM more frequently for 2 weeks when starting or stopping NNRTI therapy.
HCV PIs ("-previr" drugs) [Kaur, et al. 2015; Yeh 2015; Mak, et al. 2018]	ETR may decrease levels of HCV PIs through induction of CYP3A.	Do not coadminister HCV PIs with ETR.
Sofosbuvir/velpatasvir (available as coformulated product) [Greig 2016]	ETR may decrease levels of velpatasvir through induction of CYP3A and (weak) inhibition of P-gP.	Do not coadminister sofosbuvir/velpatasvir with ETR.
Daclatasvir [Garrison, et al. 2018]	ETR induces CYP3A, lowering daclatasvir levels.	Increase dose of daclatasvir to 90 mg per day.
Atazanavir (ATV) [Orrell, et al. 2015; Marzolini, et al. 2016]	• ETR is a substrate and inducer of CYP3A4. • COBI is a substrate and inhibitor of CYP3A4. • ATV is a substrate and inhibitor of CYP3A4.	• Use with RTV-boosted ATV results in decreases in ATV exposure, but the decrease is not considered relevant and ETR and RTV-boosted ATV can be administered together without dose adjustments. • Due to the potential for decreased ARV efficacy, avoid use of ETR with COBI. When these medications are given together, the concentrations of COBI are decreased. • When possible, avoid concomitant use of ETR and unboosted ATV. ETR with unboosted ATV results in significant decreases in ATV exposure.
Dolutegravir (DTG) [Green, et al. 2017]	• ETR induces UGT1A1 and CYP3A enzymes. • DTG is a substrate of UGT1A1 and CYP3A enzymes.	ETR reduces concentrations of DTG. Do not use concomitantly unless a boosted PI is also a part of the treatment regimen.
Rifabutin, rifampin	• **Rifabutin:** When used concomitantly with ETR, increased rifabutin levels are expected and decreased ETR levels may be seen. • **Rifampin** induction of CYP3A reduces bioavailability of ETR.	• **Rifabutin:** If ETR and rifabutin are used concomitantly, rifabutin should be dosed at 300 mg daily, with no changes to the dose of ETR. Continue this dosing until at least 2 weeks after rifabutin is stopped. – Concomitant use of a boosted PI with ETR and rifabutin is contraindicated. • **Rifampin:** Concomitant use is contraindicated.

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Gender-affirming hormones	• **Estradiol:** ETR could induce CYP3A and could decrease estradiol levels. • **Finasteride, testosterone:** Levels may decrease when taken concomitantly with ETR.	• **Estradiol:** No dose adjustments are recommended, but when taken concomitantly with ETR, monitor for signs of estrogen deficiency or excess. • **Finasteride, testosterone:** No dose adjustments recommended.

Abbreviations: ARV, antiretroviral; COBI, cobicistat; CYP, cytochrome P450; EFV, efavirenz; HCV, hepatitis C virus; INR, international normalized ratio; NNRTI, non-nucleoside reverse transcriptase inhibitor; P-gP, P-glycoprotein; PI, protease inhibitor; RTV, ritonavir; UGT, uridine diphosphate glucuronosyltransferase.

No significant interactions/no dose adjustments necessary: Common oral antibiotics (Table 15); acid-reducing agents (Table 21); polyvalent cations (Table 22); asthma and allergy medications (Table 23); long-acting beta agonists (Table 24); non-opioid pain medications (Table 31); opioid analgesics and tramadol (Table 32); alcohol, disulfiram, and acamprosate (Table 36).