

Table 13: Etravirine (ETR) Interactions (also see prescribing information)

Class or Drug	Mechanism of Action	Clinical Comments
Aliskiren	ETR is a minor inhibitor of P-gP and may minimally increase aliskiren concentrations, but this has not been studied.	When using with ETR, monitor for aliskiren-related adverse effects; switch to alternative antihypertensive medicine or ARV if necessary.
Warfarin	Metabolism of warfarin could potentially increase (or more rarely decrease).	Use cautiously with warfarin; if use is necessary, increase INR monitoring. • If INR increases, decrease warfarin dose. • If INR decreases, increase warfarin dose slowly.
Antiplatelet medications [Kakuda, et al. 2011; Rathbun and Liedtke 2010]	• Cilostazol: ETR may reduce cilostazol concentrations. • Dipyridamole: ETR may induce UGT enzymes, which are responsible for metabolism. • Ticagrelor, clopidogrel: ETR reduces ticagrelor concentrations and conversion of clopidogrel to its active metabolite. • Vorapaxar: When coadministered with ETR, vorapaxar levels expected to be reduced.	• Cilostazol: Monitor for antiplatelet effect; may be necessary to use alternative antiplatelet medication or alternative ARV. • Dipyridamole: Monitor for antiplatelet effect; use another ARV if necessary. • Ticagrelor, clopidogrel: Use with ETR may reduce antiplatelet effect; monitor closely for efficacy and use alternative ARV if possible. • Prasugrel: When coadministered with ETR, no dose adjustments are necessary. • Vorapaxar: No data available.
Statins	• Simvastatin, lovastatin: ETR may decrease concentrations. • Atorvastatin, pravastatin, fluvastatin: ETR 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 for cholesterol-lowering effect of statins. May require increased dose if necessary.
Saxagliptin, sitagliptin	ETR may decrease concentrations.	Monitor for efficacy; if necessary, increase dose of DPP-4 inhibitor.
Inhaled and injected corticosteroids	Coadministration may reduce corticosteroid concentrations.	Dexamethasone (systemic): Consider alternative corticosteroid for long-term use; if benefits of use outweigh risks, monitor for virologic response.
Trazodone	ETR may decrease trazodone concentrations.	Monitor for antidepressant and/or sedative effects.
Bupropion	No significant interactions are expected.	Monitor for clinical effect and increase as needed, but do not exceed recommended maximum dose.
Alprazolam	ETR may reduce alprazolam concentrations.	Monitor for benzodiazepine withdrawal.
Diazepam	ETR may reduce diazepam concentrations.	No dose adjustments are necessary.

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Sleep medications	Zolpidem: ETR may reduce zolpidem concentrations.	• Zolpidem, eszopiclone: Monitor for efficacy; no dose adjustments are recommended. • Suvorexant: Monitor for efficacy; do not exceed 20 mg per day.
Antipsychotics	• Aripiprazole, brexpiprazole: ETR may decrease aripiprazole and brexpiprazole concentrations. • Risperidone: ETR may decrease risperidone efficacy.	Aripiprazole, brexpiprazole, risperidone: Titrate slowly to achieve clinical effect; monitor for efficacy and adverse effects.
Carbamazepine, oxcarbazepine, phenobarbital, phenytoin	Coadministration may significantly reduce concentrations of ARVs 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 TDM if use cannot be avoided.
Lamotrigine, zonisamide	ETR may reduce lamotrigine or zonisamide efficacy.	Titrate slowly to achieve clinical effect; monitor for efficacy.
Hormonal contraceptives	Information is based on what is known with EFV drug interactions.	• Etonogestrel: No data available; consider alternative or additional contraceptive methods or alternative ARV. • Ulipristal: Monitor closely for reduced efficacy.
Erectile and sexual dysfunction agents	• PDE5 inhibitors: ETR may reduce effectiveness of PDE5 inhibitors (sildenafil, vardenafil, and tadalafil). • Flibanserin: ETR may reduce flibanserin concentrations.	• PDE5 inhibitors: Monitor for clinical effect; if dose increase is needed to achieve desired clinical effect, titrate under medical supervision to lowest effective dose. • Flibanserin: Do not coadminister.
Buprenorphine	No significant interactions are expected.	Titrate opioid or antagonist as required to achieve clinical effect; monitor for signs of withdrawal or opioid toxicity.
Methadone	ETR may slightly increase methadone concentrations.	• Titrate opioid or antagonist as required to achieve clinical effect; monitor for signs of withdrawal or opioid toxicity. • Monitor for signs of methadone toxicity; reduce dose if necessary.
Cyclosporine, tacrolimus	ETR may lower concentrations.	• Adjust cyclosporine and tacrolimus dose based on efficacy and TDM. • Conduct TDM more frequently for 2 weeks when starting or stopping NNRTI therapy.
HCV PIs (“-previr” drugs) [Mak, et al. 2018; Kaur, et al. 2015; Yeh 2015]	ETR may decrease HCV PI levels through CYP3A induction.	Do not coadminister.

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Sofosbuvir/velpatasvir (available as coformulated product) [Greig 2016]	ETR may decrease velpatasvir levels through CYP3A induction and (weak) P-gP inhibition.	Do not coadminister.
Daclatasvir [Garrison, et al. 2018]	ETR induces CYP3A, lowering daclatasvir levels.	Increase dose of daclatasvir to 90 mg per day.
Atazanavir (ATV) [Marzolini, et al. 2016; Orrell, et al. 2015]	- ETR is a substrate and inducer of CYP3A4. - COBI and ATV are substrates and inhibitors of CYP3A4.	- Administration with RTV-boosted ATV results in decreased ATV exposure, but decrease is not considered relevant; no dose adjustments are necessary. - Due to potential for decreased ARV efficacy, avoid use of ETR with COBI. When these medications are given together, COBI concentrations 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 DTG concentrations. Do not use concomitantly unless boosted PI is also part of treatment regimen.
Lenacapavir (LEN)	CYP3A4 and P-gP induction associated with concomitant HIV treatment potentially decreases LEN levels.	Do not coadminister.
Rifabutin, rifampin, rifapentine	Rifabutin: When used concomitantly, increased rifabutin levels are expected and decreased ETR levels may occur. Rifampin, rifapentine: CYP3A induction reduces ETR bioavailability.	Rifabutin: - If ETR and rifabutin are used concomitantly, dose rifabutin at 300 mg daily, with no changes to ETR dose. Continue rifabutin 300 mg daily dosing until at least 2 weeks after rifabutin is stopped. - Concomitant use of boosted PI with ETR and rifabutin is contraindicated. Rifampin, rifapentine: Concomitant use is contraindicated.
Mpox treatments	Tecovirimat is a weak inducer of CYP3A and a weak inhibitor of CYP2C8 and CYP2C19; use may 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.
Gender-affirming hormones	Estradiol: ETR may reduce estradiol levels via CYP3A induction. Finasteride, dutasteride: ETR may reduce finasteride and dutasteride levels via CYP3A induction. Progestins (oral medroxyprogesterone, micronized progesterone): ETR may reduce progestin levels via CYP3A induction. Testosterone: ETR may reduce testosterone levels via CYP3A induction.	Estradiol: Monitor serum estradiol levels; may require increased estradiol dose. Finasteride, dutasteride, progestins (oral medroxyprogesterone, micronized progesterone), testosterone: No dose adjustments are necessary.

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ADHD medications	Modafinil: CYP3A4 induction may reduce NNRTI levels.	Modafinil: Avoid concurrent use due to potential loss of virologic response.
Abbreviations: ADHD, attention-deficit/hyperactivity disorder; ARV, antiretroviral; COBI, cobicistat; CYP, cytochrome P450; DPP-4, dipeptidyl peptidase-4; EFV, efavirenz; HCV, hepatitis C virus; INR, international normalized ratio; NNRTI, non-nucleoside reverse transcriptase inhibitor; P-gP, P-glycoprotein; PDE5, phosphodiesterase type 5; PI, protease inhibitor; RTV, ritonavir; TDM, therapeutic drug monitoring; UGT, uridine diphosphate glucuronosyltransferase; VIGIV, vaccinia immune globulin intravenous. No significant interactions/no dose adjustments necessary (see guideline section Drug-Drug Interactions by Common Medication Class): Common oral antibiotics; acid-reducing agents; polyvalent cations; asthma and allergy medications; long-acting beta agonists; nonopioid pain medications; opioid analgesics and tramadol; alpha-adrenergic antagonists for benign prostatic hyperplasia; alcohol, disulfiram, and acamprosate; COVID-19 therapeutics.		

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