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<tr>
<td>Antacids</td>
<td>EVG chelates with polyvalent cations, which may reduce the efficacy of both agents.</td>
<td>Administer at least 2 hours before or 6 hours after EVG.</td>
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| Factor Xa inhibitors [Egan, et al. 2014] | • Factor Xa inhibitors are substrates of P-gp and CYP3A.  
• COBI inhibits P-gp and CYP3A.  
• May increase concentrations, increasing bleeding risk. | • Rivaroxaban, edoxaban: Avoid concomitant use.  
• Apixaban: Reduce apixaban dose to 2.5 mg twice per day, and if patient is already taking 2.5 mg twice per day, avoid concomitant use.  
• Dabigatran: In patients with good renal function, no dose adjustments are necessary.  
• Do not use this combination in patients with moderate to severe renal dysfunction. |
| Warfarin      | Could potentially decrease (or more rarely) increase metabolism of warfarin. | • Use cautiously with warfarin, and if use is necessary, increase monitoring of INR.  
• Decrease dose if INR increases. Increase dose slowly if INR decreases. |
• Ticagrelor: Results in increased exposure to ticagrelor.  
• Clopidogrel: Results in decreased concentration of clopidogrel’s active metabolite. | • Cilostazol: Monitor for antiplatelet effect. May be necessary to use an alternative antiplatelet drug or alternative ARV agent.  
• Ticagrelor: Do not use with boosted EVG.  
• Clopidogrel: Do not use with boosted EVG unless an alternative antiplatelet drug (or ARV agent) cannot be used. |
| Aliskiren     | COBI inhibits P-gp, which may decrease aliskiren elimination, increasing risk of adverse events. | Do not coadminister. |
| Other polyvalent cations (calcium, zinc, iron, etc.) | EVG chelates with polyvalent cations. | Administer at least 2 hours before or 6 hours after EVG. |
| Atenolol      | COBI-boosted EVG may increase atenolol concentrations via inhibition of MATE-1 elimination. | • Start patient at lowest possible dose and monitor for adverse events before slowly increasing dose to effect.  
• If patient is already taking atenolol but starting a cobicistat-boosted EVG, monitor for atenolol-related adverse events. Reduce dose of atenolol as needed. |
| Calcium channel blockers (CCBs) | COBI-boosted EVG may increase CCB concentrations by as much as 50%. | Decrease the original dose of CCB by up to 50% when using with boosted EVG and slowly titrate to effect. |
| Eplerenone [Keating and Plosker 2004; Tseng, et al. 2017] | • Eplerenone is metabolized by CYP3A.  
• COBI inhibits CYP3A. | • Avoid concomitant use (increased risk of hyperkalemia and hypertension).  
• If concomitant use is required, use lowest possible effective dose of eplerenone. |
| Simvastatin, lovastatin [Perry 2014] | • COBI is an inhibitor of CYP3A.  
• Simvastatin and lovastatin are substrates of CYP3A.  
• Greatly increases concentrations. | Avoid concomitant use (may increase muscle aches and risk of rhabdomyolysis). |
## Boosted Elvitegravir (EVG) Interactions (also see drug package inserts)

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• COBI inhibits OATP1B1.  
• Although moderate increases are possible, low doses are considered safe when used with boosted PIs.                                                                 | • Use the lowest effective dose of pitavastatin and monitor for signs of toxicity, including myopathy.  
• Dose adjustments are not necessary when using these statins with boosted EVG.                                                                                                           |
• COBI inhibits OATP1B1.  
• Although moderate increases are possible, low doses are considered safe when used with boosted PIs.                                                                 | • Use the lowest effective dose of pravastatin and monitor for signs of toxicity, including myopathy.  
• Dose adjustments are not necessary when using these statins with boosted EVG.                                                                                                           |
• Boosted EVG inhibits both CYP3A and OATP1B1.  
• May moderately increase concentrations.                                                                                                                                     | • Avoid concomitant use of cobicistat and atorvastatin.  
• If atorvastatin use is necessary, do not exceed 20 mg per day.                                                                                                                                                                        |
| Rosuvastatin [Custodio, et al. 2014] | • Rosuvastatin is a substrate of OATP1B1 and OATP1B3.  
• COBI inhibits OATP.  
• Rosuvastatin is a substrate of CYP2C9.  
• EVG is an inducer of CYP2C9.  
• May moderately increase concentrations.                                                                                                                                            | • When possible, avoid concomitant use of rosuvastatin and COBI-boosted EVG.  
• If rosuvastatin use is necessary, start with 10 mg per day. Dose should not exceed 20 mg per day.                                                                                                                                       |
| Fluvastatin                   | Interaction has not been studied, but potential for moderate increase is possible.                                                                                                                                  | Do not use, but if clinical use is desired, use the lowest effective dose; monitor closely for safety and efficacy before increasing statin dose.                                                                                          |
| Antidiabetic drugs            | • Metformin: COBI is known to inhibit MATE1, which plays a role in the elimination of metformin, thus increasing metformin concentrations.  
• Glyburide: Mainly metabolized by CYP3A; concentrations are increased by inhibitors of this enzyme.  
• Saxagliptin: Levels may be increased via inhibition of CYP3A.  
• Canagliflozin: Could lead to reduced canagliflozin exposure because of EVG’s induction of UGT enzymes.                                                                 | • Metformin: Monitor for metformin-related adverse events and reduce dose as needed.  
• Glyburide or alternative sulfonylureas: Use lowest effective doses with boosted EVG; monitor for signs of hypoglycemia.  
• Saxagliptin: Limit dose to 2.5 mg once per day.  
• Canagliflozin: Monitor glycemic control. With RTV-boosted EVG and inadequate glycemic control, consider increasing dose to 300 mg per day if patient is tolerating 100 mg and has GFR >60 ml/min/1.73m². |
| Long-acting beta agonists (formoterol, salmeterol, etc.) | • Inhibition of CYP3A increases plasma concentrations of these agents.  
• Increased risk of salmeterol-associated cardiovascular events.                                                                                                                                                  | • Concomitant use is contraindicated unless benefits outweigh risks; consider use of alternative ARV agents.  
• If coadministration is necessary, monitor frequently for QT prolongation, palpitations, and sinus tachycardia.                                                                                                                  |
### Boosted Elvitegravir (EVG) Interactions (also see drug package inserts)

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| Inhaled and injected corticosteroids   | Risk of Cushing’s syndrome when coadministered with the following:                 | **Intrasanal or inhaled fluticasone, mometasone, ciclesonide, budesonide, and triamcinolone:** Do not coadminister unless potential benefits outweigh risk; consider alternative corticosteroid (e.g., beclomethasone).  
**Systemic betamethasone, budesonide:** Do not coadminister unless benefits outweigh risk.  
**Systemic prednisolone, prednisone:** Do not coadminister unless potential benefits outweigh risk; if use cannot be avoided, use for shortest effective duration.  
**Injectable betamethasone, triamcinolone:** Do not coadminister unless benefits outweigh risk.  
**Systemic dexamethasone:** Do not coadminister unless potential benefits outweigh risk; consider alternative corticosteroid. |
|                                        | • **Intrasanal or inhaled:** Fluticasone, mometasone, ciclesonide, budesonide, triamcinolone.  
• **Systemic:** Betamethasone, budesonide, prednisolone, prednisone, dexamethasone.  
• **Injectable:** Betamethasone, triamcinolone. |
| Trazodone                              | May increase trazodone concentrations.                                              | **Quetiapine:** Reduce dose to 1/6 if initiating ARVs in patients on stabilized quetiapine.  
Use all other antipsychotics at the lowest dose possible in patients taking boosted ARVs, and careful monitoring for adverse events is warranted. |
| Alprazolam, clonazepam, diazepam       | These benzodiazepines are substrates of CYP3A and may be increased in the presence of strong inhibitors of this enzyme. | **Consider alternative benzodiazepine (e.g., lorazepam, oxazepam, temazepam).  
If used, administer lowest effective dose; monitor closely for adverse events. |
| Antipsychotics                         | Several of these agents are substrates of CYP3A, and inhibitors of this enzyme may increase their concentrations. | **Quetiapine:** Reduce dose to 1/6 if initiating ARVs in patients on stabilized quetiapine.  
Use all other antipsychotics at the lowest dose possible in patients taking boosted ARVs, and careful monitoring for adverse events is warranted. |
| PDE5 inhibitors [Perry 2014]           | • COBI is an inhibitor of CYP3A.  
• PDE5 inhibitors are substrates of CYP3A.  
• **Flibanserin:** Increased flibanserin concentrations expected. | **Avoid concomitant use or use with lowest effective dose of the PDE5 inhibitor (may increase risk of hypotension, syncpe, priapism, and other adverse reactions).**  
**Sildenafil:** Start with 25 mg every 48 hours; monitor for adverse effects.  
**Tadalafil:** Start with 5 mg; do not exceed 10 mg every 72 hours; monitor for adverse effects.  
**Vardenafil:** Administer 2.5 mg every 72 hours; monitor for adverse effects.  
**Flibanserin:** Coadministration is contraindicated. |
| Suvorexant [Kishi, et al. 2015]        | • Suvorexant is a CYP3A substrate.  
• COBI is an inhibitor of CYP3A. |
| Zolpidem, eszopiclone                  | These drugs are CYP3A substrates and may be increased by strong inhibitors of this enzyme. | Avoid concomitant use or use the lowest effective dose (may increase somnolence, dizziness, and risk of sleep hangover).  
**Zolpidem:** Administer lowest possible dose of zolpidem and monitor for adverse events.  
**Eszopiclone:** Start with 1 mg of eszopiclone at bedtime and titrate slowly for maximum effect. |
| 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. |
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<td>Eletriptan</td>
<td>Eletriptan is a CYP3A substrate and concentrations may be increased if given with strong inhibitors of this enzyme.</td>
<td>Do not coadminister. Select an alternative triptan medication.</td>
</tr>
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<td>Opioid analgesics</td>
<td>Complex mechanisms of metabolism and formation of both active and inactive metabolites create interactions of unclear significance between these drugs and boosted EVG.</td>
<td>Monitor for signs of opiate toxicity and analgesic effect and dose these analgesics accordingly.</td>
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<td>Tramadol</td>
<td>Tramadol exposure is increased with inhibition of CYP3A, but this reduces conversion to the more potent active metabolite seen when tramadol is metabolized by CYP2D6.</td>
<td>When tramadol is given with COBI or RTV, monitoring for tramadol-related side effects and for the analgesic effect may be required as clinically indicated; adjust tramadol dosage if needed.</td>
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| Hormonal contraceptives | **Drospirenone:** Potential for hyperkalemia.                                             | • **Ethinyl estradiol, norgestimate, metabolites; norethindrone:** Weigh risks/benefits; consider alternative contraceptive method.  
  • **Drospirenone:** Monitor for hyperkalemia; consider alternative contraceptive or alternative ARV agent.  
  • **Etonogestrel:** No data; consider alternative or additional contraceptive or alternative ARV agent.  

| Immunosuppressants   | • **Everolimus, sirolimus:** Metabolism decreased by boosted EVG.  
  • **Cyclosporine, tacrolimus:** Metabolism decreased by boosted EVG. | • **Everolimus, sirolimus:** Do not use with boosted EVG.  
  • **Cyclosporine, tacrolimus:** Dose based upon therapeutic drug monitoring.  
  • Monitor closely for adverse events. |

**Abbreviations:** ARV, antiretroviral; COBI, cobicistat; CYP, cytochrome P450; GFR, glomerular filtration rate; INR, international normalized ratio; MATE, multidrug and toxin extrusion; OATP, organic anion transporting polypeptide; P-gP, P-glycoprotein; PI, protease inhibitor; RTV, ritonavir; UGT, uridine glucuronosyltransferase.

**No significant interactions/no dose adjustments necessary:** Common oral antibiotics; acid-reducing agents; asthma and allergy medications; tobacco and smoking cessation products; alcohol, disulfiram, and acamprosate; methadone, buprenorphine, naloxone, and naltrexone.

**References**


