Table 18b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017)

This table provides information relating to PK interactions between NNRTIs and non-ARV drugs. For interactions between ARV agents and for dosing recommendations, refer to Tables 18c, 19a, and 19b. Recommendations for managing a particular drug interaction may differ depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or if a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly.

Note: Delavirdine (DLV) is not included in this table. Please refer to the DLV Food and Drug Administration package insert for information regarding drug interactions.

<table>
<thead>
<tr>
<th>Concomitant Drug Class/ Name</th>
<th>NNRTIa</th>
<th>Effect on NNRTI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acid Reducers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antacids</td>
<td>RPV</td>
<td>↓ RPV expected when given simultaneously</td>
<td>Give antacids at least 2 hours before or at least 4 hours after RPV.</td>
</tr>
<tr>
<td>H2 Receptor Antagonists</td>
<td>RPV</td>
<td>↓ RPV</td>
<td>Give H2 receptor antagonists at least 12 hours before or at least 4 hours after RPV.</td>
</tr>
<tr>
<td>PPIs</td>
<td>RPV</td>
<td>With Omeprazole 20 mg Daily: • RPV AUC ↓ 40%, Cmin ↓ 33%</td>
<td>Contraindicated. Do not coadminister.</td>
</tr>
<tr>
<td>Anticoagulants/Antiplaetelets</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apixaban</td>
<td>EFV, ETR, NVP</td>
<td>↓ apixaban possible</td>
<td>Consider alternative therapy.</td>
</tr>
<tr>
<td>Betrixaban</td>
<td>EFV, NVP, RPV, ETR</td>
<td>↔ betrixaban expected</td>
<td>No dose adjustment necessary. Consider alternative therapy. If coadministration is necessary, monitor for betrixaban toxicity.</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>ETR</td>
<td>↓ activation of clopidogrel possible</td>
<td>ETR may prevent metabolism of clopidogrel (inactive) to its active metabolite. Avoid coadministration, if possible.</td>
</tr>
<tr>
<td>NVP, RPV</td>
<td>↔ clopidogrel expected</td>
<td></td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Dabigatran</td>
<td>EFV, NVP, RPV, ETR</td>
<td>↔ dabigatran expected</td>
<td>No dose adjustment necessary. Consider alternative therapy. If coadministration is necessary, monitor for dabigatran toxicity.</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>EFV, NVP, RPV, ETR</td>
<td>↔ edoxaban expected</td>
<td>No dose adjustment necessary. Consider alternative therapy. If coadministration is necessary, monitor for edoxaban toxicity.</td>
</tr>
<tr>
<td>Prasugrel</td>
<td>EFV, ETR, NVP, RPV</td>
<td>↔ prasugrel expected</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>EFV, ETR, NVP</td>
<td>↓ rivaroxaban possible</td>
<td>Consider alternative therapy.</td>
</tr>
<tr>
<td>Ticagrelor</td>
<td>EFV, ETR, NVP</td>
<td>↓ ticagrelor expected</td>
<td>Consider alternative therapy.</td>
</tr>
<tr>
<td>Warfarin</td>
<td>EFV, ETR, NVP</td>
<td>↑ or ↓ warfarin possible</td>
<td>Monitor INR and adjust warfarin dose accordingly.</td>
</tr>
<tr>
<td>Concomitant Drug Class/Name</td>
<td>NNRTI(^a)</td>
<td>Effect on NNRTI and/or Concomitant Drug Concentrations</td>
<td>Dosing Recommendations and Clinical Comments</td>
</tr>
<tr>
<td>----------------------------</td>
<td>------------</td>
<td>------------------------------------------------------</td>
<td>------------------------------------------------</td>
</tr>
<tr>
<td><strong>Anticonvulsants</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Carbamazepine, Phenobarbital, Phenytoin | EFV | Carbamazepine + EFV:  
- Carbamazepine AUC ↓ 27%  
- EFV AUC ↓ 36%  
Phenytoin + EFV:  
- ↓ EFV  
- ↓ phenytoin possible | Monitor anticonvulsant and EFV levels or, if possible, use alternative anticonvulsant to those listed. |
|                            | ETR | ↓ anticonvulsant and ETR possible | **Do not coadminister.** Consider alternative anticonvulsant. |
|                            | NVP | ↓ anticonvulsant and NVP possible | Monitor anticonvulsant and NVP levels and virologic responses or consider alternative anticonvulsant. |
|                            | RPV | ↓ RPV possible | **Contraindicated. Do not coadminister.** Consider alternative anticonvulsant. |
| Eslicarbazepine             | EFV, ETR, NVP, RPV | ↓ NNRTI possible | Monitor virologic outcomes and consider monitoring plasma concentrations of ARVs, or consider alternative anticonvulsant or ARV drug. |
| Oxcarbazepine               | RPV | ↓ RPV possible | **Contraindicated. Do not coadminister.** Consider alternative anticonvulsant. |
| Ethosuximide, Lacosamide, Tiagabine, Zonisamide, | ETR, EFV | ↓ anticonvulsant possible | Monitor seizure control and plasma concentrations of anticonvulsants (when available). |
| Lamotrigine                 | EFV | ↓ lamotrigine possible | Monitor seizure control and plasma concentrations of lamotrigine. |
| **Antidepressants**         |            |                                                      |                                                 |
| Bupropion                   | EFV, NVP | Bupropion AUC ↓ 55%  
↓ bupropion possible | Titrate bupropion dose based on clinical response. |
| Citalopram, Escitalopram    | EFV, ETR, NVP | ↓ antidepressant possible | Titrate antidepressant dose based on clinical response. |
| Fluoxetine, Fluvoxamine     | EFV, ETR, NVP, RPV | ↔ antidepressant expected | No dose adjustment necessary. |
| Paroxetine                  | EFV, ETR, NVP, RPV | ↔ paroxetine observed with EFV or ETR  
↔ expected with NVP or RPV | No dose adjustment necessary. |
| Nefazodone                  | EFV, ETR, NVP, RPV | ↓ nefazodone expected  
↑ NNRTI possible  
↑ RPV possible | Monitor the antidepressant effect and titrate dose as necessary. Monitor for ARV-related adverse events. |
| Sertraline                  | EFV | Sertraline AUC ↓ 39% | Titrate sertraline dose based on clinical response. |
| Trazodone                   | EFV, ETR, NVP | ↓ trazodone possible | Monitor the therapeutic effect of trazodone and titrate dose as necessary. |
### Table 18b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017)  (page 3 of 9)

<table>
<thead>
<tr>
<th>Concomitant Drug Class/ Name</th>
<th>NNRTI(^a)</th>
<th>Effect on NNRTI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antifungals</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluconazole</td>
<td>EFV</td>
<td>↔ fluconazole or EFV</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>ETR</td>
<td>ETR AUC ↑ 86%</td>
<td></td>
<td>No dose adjustment necessary. Use with caution.</td>
</tr>
<tr>
<td>NVP</td>
<td>NVP AUC ↑ 110%</td>
<td></td>
<td>Increased risk of hepatotoxicity possible with this combination. Monitor NVP toxicity or use alternative ARV agent.</td>
</tr>
<tr>
<td>RPV</td>
<td>↑ RPV possible</td>
<td></td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Isavuconazole</td>
<td>EFV, ETR, NVP</td>
<td>↓ isavuconazole possible</td>
<td>Dose adjustments for isavuconazole may be necessary. Consider monitoring isavuconazole level and antifungal response.</td>
</tr>
<tr>
<td></td>
<td>RPV ↑ RPV possible</td>
<td></td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Itraconazole</td>
<td>EFV</td>
<td>Itraconazole and OH-itraconazole AUC, C(<em>{max}), and C(</em>{min}) ↓ 35%–44%</td>
<td>Failure to achieve therapeutic itraconazole concentrations has been reported. Avoid this combination if possible. If coadministered, closely monitor itraconazole concentration and adjust dose accordingly.</td>
</tr>
<tr>
<td>ETR</td>
<td>↓ itraconazole possible</td>
<td></td>
<td>Dose adjustments for itraconazole may be necessary. Monitor itraconazole level and antifungal response.</td>
</tr>
<tr>
<td></td>
<td>↑ ETR possible</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NVP</td>
<td>Itraconazole AUC ↓ 61%</td>
<td></td>
<td>Avoid this combination if possible. If coadministered, monitor itraconazole concentration and adjust dose accordingly.</td>
</tr>
<tr>
<td></td>
<td>↑ NVP possible</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RPV</td>
<td>↑ RPV possible</td>
<td></td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Posaconazole</td>
<td>EFV</td>
<td>Posaconazole AUC ↓ 50% ↔ EFV</td>
<td>Avoid concomitant use unless the benefit outweighs the risk. If coadministered, monitor posaconazole concentration and adjust dose accordingly. Monitor for NNRTI toxicities.</td>
</tr>
<tr>
<td>ETR, NVP, RPV</td>
<td>↑ NNRTI possible</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Voriconazole</td>
<td>EFV</td>
<td>Voriconazole AUC ↓ 77% EFV AUC ↑ 44%</td>
<td><strong>Contraindicated at standard doses.</strong></td>
</tr>
<tr>
<td>ETR</td>
<td>Voriconazole AUC ↑ 14%</td>
<td></td>
<td>Dose Adjustment:</td>
</tr>
<tr>
<td></td>
<td>ETR AUC ↑ 36%</td>
<td></td>
<td>• Voriconazole 400 mg BID, EFV 300 mg daily</td>
</tr>
<tr>
<td>NVP</td>
<td>↓ voriconazole possible</td>
<td></td>
<td>No dose adjustment necessary; use with caution. Consider monitoring voriconazole level. Monitor for toxicity and antifungal response and/or voriconazole level.</td>
</tr>
<tr>
<td></td>
<td>↑ NVP possible</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RPV</td>
<td>↑ RPV possible</td>
<td></td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td><strong>Antihyperglycemics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canagliflozin, Dapagliflozin, Empagliflozin, Sitagliptin</td>
<td>EFV, ETR, NVP, RPV</td>
<td>↔ antihyperglycemic expected</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Linagliptin, Saxagliptin</td>
<td>EFV, ETR, NVP</td>
<td>↓ antihyperglycemic possible</td>
<td>Monitor glycemic control.</td>
</tr>
</tbody>
</table>
Table 18b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs *(Last updated October 17, 2017; last reviewed October 17, 2017)* *(page 4 of 9)*

<table>
<thead>
<tr>
<th>Concomitant Drug Class/ Name</th>
<th>NNRTI</th>
<th>Effect on NNRTI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antimalarials</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Artemether/ Lumefantrine</td>
<td>EFV</td>
<td>Artemether AUC ↓ 79%</td>
<td>Consider alternative ARV or antimalarial drug. If used in combination, monitor closely for antimalarial efficacy and malaria recurrence.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DHA AUC ↓ 75%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lumefantrine AUC ↓ 56%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>Artemether AUC ↓ 38%</td>
<td>Clinical significance of the reduced antimalarial drug concentrations unknown. If used in combination with ETR, monitor closely for antimalarial efficacy.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DHA AUC ↓ 15%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lumefantrine AUC ↓ 13%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>ETR AUC ↑ 10%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>Artemether AUC ↓ 67%–72%</td>
<td>Clinical significance unknown. If used, monitor closely for antimalarial efficacy and lumefantrine toxicity.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DHA: Study results are conflicting. AUC ↓ 37% in one study, no difference in another. Lumefantrine: Study results are conflicting. Lumefantrine AUC ↓ 25%–58% in 2 studies but ↑ 56% in another.</td>
<td></td>
</tr>
<tr>
<td>Atovaquone/ Proguanil</td>
<td>EFV</td>
<td>Atovaquone AUC ↓ 75%</td>
<td>No dose recommendation. Consider alternative drug for malaria prophylaxis, if possible.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Proguanil AUC ↓ 43%</td>
<td></td>
</tr>
<tr>
<td>Antimycobacterials</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bedaquiline</td>
<td>EFV, ETR</td>
<td>↓ bedaquiline possible</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>↔ bedaquiline AUC</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>EFV</td>
<td>Clarithromycin AUC ↓ 39%</td>
<td>Monitor for effectiveness or consider alternative agent, such as azithromycin, for MAC prophylaxis and treatment.</td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>Clarithromycin AUC ↓ 39%</td>
<td>Consider alternative agent, such as azithromycin, for MAC prophylaxis and treatment.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ETR AUC ↑ 42%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>Clarithromycin AUC ↓ 31%</td>
<td>Monitor for effectiveness or use alternative agent, such as azithromycin, for MAC prophylaxis and treatment.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NVP AUC ↑ 26%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>↔ clarithromycin expected</td>
<td>Consider alternative macrolide, such as azithromycin, for MAC prophylaxis and treatment.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ RPV possible</td>
<td></td>
</tr>
</tbody>
</table>
| Rifabutin                    | EFV   | Rifabutin ↓ 38%                                       | **Dose:**  
|                              |       |                                                        | • Rifabutin 450–600 mg/day; or  
|                              |       |                                                        | • Rifabutin 600 mg 3 times/week if EFV is not coadministered with a PI. |
|                              | ETR   | Rifabutin and metabolite AUC ↓ 17%                    | If ETR is used with an RTV-boosted PI, rifabutin should not be coadministered. **Dose:**  
|                              |       | ETR AUC ↓ 37%                                         | • Rifabutin 300 mg once daily if ETR is not coadministered with a PI/r. |

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Table 18b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs *(Last updated October 17, 2017; last reviewed October 17, 2017)* *(page 5 of 9)*

<table>
<thead>
<tr>
<th>Concomitant Drug Class/ Name</th>
<th>NNRTIa</th>
<th>Effect on NNRTI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antimycobacterials</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rifabutin, continued</td>
<td>NVP</td>
<td>Rifabutin AUC ↑ 17% and metabolite AUC ↑ 24%</td>
<td>No dose adjustment necessary. Use with caution.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NVP C_{min} ↓ 16%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>Rifabutin + RPV 50 mg once daily compared to RPV 25 mg once daily alone: ↔ RPV AUC, C_{min}</td>
<td>Increase RPV dose to 50 mg once daily.</td>
</tr>
<tr>
<td><strong>Rifampin</strong></td>
<td>EFV</td>
<td>EFV AUC ↓ 26%</td>
<td>Maintain EFV dose at 600 mg once daily and monitor for virologic response. Consider therapeutic drug monitoring.</td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>Significant ↓ ETR possible</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>NVP ↓ 20%–58%</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>RPV AUC ↓ 80%</td>
<td><strong>Contraindicated. Do not coadminister.</strong></td>
</tr>
<tr>
<td><strong>Rifapentine</strong></td>
<td>EFV</td>
<td>↔ EFV concentrations</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td>ETR, NVP</td>
<td>↓ NNRTI possible</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>↓ RPV expected</td>
<td><strong>Contraindicated.</strong></td>
</tr>
<tr>
<td><strong>Antipneumocystis and Antitoxoplasmosis Drugs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atovaquone</td>
<td>EFV</td>
<td>Atovaquone AUC ↓ 44%–47%</td>
<td>Consider alternative agent for PCP or toxoplasmosis treatment or use alternative ARV drug. If used in combination, monitor therapeutic efficacy of atovaquone.</td>
</tr>
<tr>
<td><strong>Antipsychotics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Olanzapine</td>
<td>EFV</td>
<td>↓ olanzapine possible</td>
<td>Monitor effect of olanzapine.</td>
</tr>
<tr>
<td></td>
<td>ETR, NVP, RPV</td>
<td>↔ olanzapine expected</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Pimozide</td>
<td>EFV</td>
<td>↑ pimozide possible</td>
<td><strong>Coadministration is not recommended. Consider alternative antipsychotic.</strong></td>
</tr>
<tr>
<td></td>
<td>ETR, NVP</td>
<td>↓ pimozide possible</td>
<td>Monitor effect of pimozide.</td>
</tr>
<tr>
<td>Lurasidone, Quetiapine, Thioridazine</td>
<td>EFV, ETR, NVP</td>
<td>↓ antipsychotic possible</td>
<td>Monitor effect of antipsychotic.</td>
</tr>
<tr>
<td><strong>Benzodiazepines</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alprazolam</td>
<td>EFV, ETR, NVP</td>
<td>↓ alprazolam possible</td>
<td>Monitor for therapeutic effectiveness of alprazolam.</td>
</tr>
<tr>
<td>Diazepam</td>
<td>EFV, NVP</td>
<td>↓ diazepam possible</td>
<td><strong>Monitor for therapeutic effectiveness of diazepam.</strong></td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>↑ diazepam possible</td>
<td>Decreased dose of diazepam may be necessary. Monitor for diazepam toxicity.</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>EFV</td>
<td>Lorazepam C_{max} ↑ 16%, AUC ↔</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Midazolam</td>
<td>EFV</td>
<td>Significant ↑ midazolam expected</td>
<td><strong>Do not coadminister with oral midazolam.</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Parenteral midazolam can be used with caution as a single dose and can be given in a monitored situation for procedural sedation.</td>
<td></td>
</tr>
<tr>
<td>Triazolam</td>
<td>EFV</td>
<td>Significant ↑ triazolam expected</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
</tbody>
</table>
Table 18b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 6 of 9)

<table>
<thead>
<tr>
<th>Concomitant Drug Class/ Name</th>
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<th>Effect on NNRTI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac Medications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dihydropyridine CCBs</td>
<td>EFV, ETR, NVP</td>
<td>↓ CCBs possible</td>
<td>Titrate CCB dose based on clinical response.</td>
</tr>
<tr>
<td>Diltiazem, Verapamil</td>
<td>EFV</td>
<td>Diltiazem AUC ↓ 69%</td>
<td>Titrate diltiazem or verapamil dose based on clinical response.</td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>↓ verapamil possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ diltiazem or verapamil possible</td>
<td></td>
</tr>
<tr>
<td>Corticosteroids</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>EFV, ETR, NVP</td>
<td>↓ EFV, ETR, and NVP possible</td>
<td>Consider alternative corticosteroid for long-term use. If dexamethasone is used with NNRTI, monitor virologic response.</td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>Significant ↓ RPV possible</td>
<td>Contraindicated with more than a single dose of dexamethasone.</td>
</tr>
<tr>
<td>Hepatitis C Direct-Acting Antiviral Agents</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daclatasvir</td>
<td>EFV, ETR, NVP</td>
<td>Daclatasvir 120 mg once daily +</td>
<td>The recommended dose is daclatasvir 90 mg once daily.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Daclatasvir 60 mg daily compared to:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>daclatasvir 60 mg alone.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>daclatasvir C&lt;sub&gt;min&lt;/sub&gt; ↓ 17%, AUC ↑ 37%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>No data</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Dasabuvir + Paritaprevir/ Ombitasivir/RTV</td>
<td>EFV</td>
<td>No data</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td></td>
<td>ETR, NVP</td>
<td>↓ DAAs possible</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>RPV AUC ↑ 150%–225%</td>
<td>Do not coadminister, due to potential for QT interval prolongation with higher concentrations of RPV.</td>
</tr>
<tr>
<td>Elbasvir/ Grazoprevir</td>
<td>EFV</td>
<td>Elbasvir AUC ↓ 54%</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td></td>
<td>ETR, NVP</td>
<td>Grazoprevir AUC ↓ 83%</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>Elbasvir, grazoprevir expected</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Glecaprevir/ Pibrentasvir</td>
<td>EFV</td>
<td>↓ glecaprevir and pibrentasvir expected</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td>NVP, ETR</td>
<td>↓ glecaprevir and pibrentasvir possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>↔ glecaprevir, pibrentasvir, and RPV ↔</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Ledipasvir/ Sofosbuvir</td>
<td>EFV</td>
<td>Ledipasvir AUC, C&lt;sub&gt;min&lt;/sub&gt;, and C&lt;sub&gt;max&lt;/sub&gt;:</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td>ETR, NVP</td>
<td>all ↓ 34%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>Sofosbuvir: no significant effect</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ledipasvir, sofosbuvir, and RPV ↔</td>
<td></td>
</tr>
<tr>
<td>Concomitant Drug Class/ Name</td>
<td>NNRTI(^a)</td>
<td>Effect on NNRTI and/or Concomitant Drug Concentrations</td>
<td>Dosing Recommendations and Clinical Comments</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>------------</td>
<td>-----------------------------------------------------</td>
<td>---------------------------------------------</td>
</tr>
<tr>
<td><strong>Hepatitis C Direct-Acting Antiviral Agents, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simeprevir</td>
<td>EFV</td>
<td>Simeprevir AUC ↓ 71%, C(_{\text{min}}) ↓ 91% ↔ EFV</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td>ETR, NVP</td>
<td>↓ simeprevir expected</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>↔ simeprevir and RPV</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir/ Velpatasvir</td>
<td>EFV</td>
<td>Velpatasvir AUC ↓ 43%, C(<em>{\text{max}}) ↓ 37% and C(</em>{\text{min}}) ↓ 47% ↔ EFV</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td>ETR, NVP</td>
<td>↓ velpatasvir expected</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>No significant effect expected</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Sofosbuvir/ Velpatasvir/ Voxilaprevir</td>
<td>EFV</td>
<td>Velpatasvir AUC ↓ 43%, C(<em>{\text{max}}) ↓ 37% and C(</em>{\text{min}}) ↓ 47% ↓ voxilaprevir expected</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td>ETR, NVP,</td>
<td>↓ voxilaprevir expected</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>No significant effect expected</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td><strong>Herbal Products</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>St. John's Wort</td>
<td>EFV, ETR, NVP, RPV</td>
<td>↓ NNRTI</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td><strong>Hormonal Therapies</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hormonal Contraceptives</td>
<td>EFV</td>
<td>Ethinyl estradiol ↔ Levonorgestrel (metabolite of oral norgestimate) AUC ↓ 83% Norelgestromin (metabolite of oral norgestimate) AUC ↓ 64% Etonogestrel (metabolite of oral desogestrel) C(_{\text{min}}) ↓ 61%</td>
<td>Use alternative or additional contraceptive methods. Unintended pregnancies were observed in women who used EFV and levonorgestrel implant concomitantly.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Etonogestrel (implant) AUC ↓ 63%–82% Levonorgestrel (implant) AUC ↓ 47%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>DMPA: no significant change</td>
<td>No dose adjustment necessary.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ethinyl estradiol AUC ↑ 22%</td>
<td>No dose adjustment necessary.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Norethindrone: no significant effect</td>
<td>Based on clinical data demonstrating no change in effectiveness, no dose adjustment necessary.</td>
<td></td>
</tr>
<tr>
<td>ETR</td>
<td>Ethinyl estradiol AUC ↓ 29%, C(_{\text{min}}) ↓ 58%</td>
<td>Based on clinical data demonstrating no change in effectiveness, no dose adjustment necessary.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Norethindrone AUC ↓ 18% Etonogestrel (metabolite of oral desogestrel) C(_{\text{min}}) ↓ 22%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Etonogestrel (implant): no significant change</td>
<td>No dose adjustment necessary.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>DMPA: no significant change</td>
<td>No dose adjustment necessary.</td>
<td></td>
</tr>
</tbody>
</table>
### Table 18b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

(Last updated October 17, 2017; last reviewed October 17, 2017) (page 8 of 9)

<table>
<thead>
<tr>
<th>Concomitant Drug Class/ Name</th>
<th>NNRTIa</th>
<th>Effect on NNRTI and/ or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hormonal Therapies, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hormonal Contraceptives, continued</strong></td>
<td>NVP, continued</td>
<td>Levonorgestrel (implant) AUC ↑ 35%</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>Ethinyl estradiol: no significant change [Norethindrone: no significant change]</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td><strong>Levonorgestrel</strong> For emergency contraception</td>
<td>EFV</td>
<td>Levonorgestrel AUC ↓ 58%</td>
<td>Effectiveness of emergency postcoital contraception may be diminished.</td>
</tr>
<tr>
<td><strong>Menopausal Hormone Replacement Therapy</strong></td>
<td>EFV, ETR, NVP</td>
<td>With estradiol or conjugated estrogen (equine and synthetic): ↓ estrogen possible [↓ medroxyprogesterone possible [↓ micronized progesterone possible [↓ drospirenone possible See Hormonal Contraceptives for other progestin-NNRTI interactions]]]</td>
<td>Monitor menopausal symptoms. The lowest dose of hormonal therapy should be used to achieve menopausal symptom relief.</td>
</tr>
<tr>
<td><strong>Gender-Affirming Hormone Therapy</strong></td>
<td>EFV, ETR, NVP</td>
<td>↓ estradiol possible [↔ goserelin, leuprolide acetate, and spironolactone expected [↓ dutasteride and finasteride possible]] [↓ testosterone possible]</td>
<td>Monitor feminizing effects of estrogen and antiandrogen therapy and adjust dosing as necessary. Monitor masculinizing effects of testosterone and adjust testosterone dose as necessary.</td>
</tr>
<tr>
<td><strong>HMG-CoA Reductase Inhibitors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>EFV, ETR</td>
<td>Atorvastatin AUC ↓ 32%–43%</td>
<td>Adjust atorvastatin according to lipid responses, but do not exceed the maximum recommended dose.</td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>↓ atorvastatin possible</td>
<td>Adjust atorvastatin according to lipid responses, not to exceed the maximum recommended dose.</td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>Atorvastatin AUC ↔ [Atorvastatin metabolites ↑ 23%–39%]</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Fluvastatin</td>
<td>EFV, ETR</td>
<td>↑ fluvastatin possible</td>
<td>Dose adjustments for fluvastatin may be necessary. Monitor for fluvastatin toxicity.</td>
</tr>
<tr>
<td>Lovastatin, Simvastatin</td>
<td>EFV</td>
<td>Simvastatin AUC ↓ 68% [Simvastatin active metabolite AUC ↓ 60%]</td>
<td>Adjust simvastatin dose according to lipid responses, but do not exceed the maximum recommended dose. If EFV is used with a PI/r, simvastatin and lovastatin should be avoided.</td>
</tr>
<tr>
<td></td>
<td>ETR, NVP</td>
<td>↓ lovastatin possible [↓ simvastatin possible]</td>
<td>Adjust lovastatin or simvastatin dose according to lipid responses, but do not exceed the maximum recommended dose. If ETR or NVP is used with a PI/r, simvastatin and lovastatin should be avoided.</td>
</tr>
</tbody>
</table>
### Table 18b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs  (Last updated October 17, 2017; last reviewed October 17, 2017)  (page 9 of 9)

<table>
<thead>
<tr>
<th>Concomitant Drug Class/ Name</th>
<th>NNRTI*</th>
<th>Effect on NNRTI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HMG-CoA Reductase Inhibitors, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pitavastatin</td>
<td>EFV</td>
<td>Pitavastatin AUC ↓ 11%, C\textsubscript{max} ↑ 20%</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td>ETR, NVP, RPV</td>
<td>← pitavastatin expected</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>EFV</td>
<td>AUC ↓ 44%</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>↓ pravastatin possible</td>
<td>Adjust statin dose according to lipid responses, but do not exceed the maximum recommended dose.</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>EFV, ETR, NVP</td>
<td>← rosvastatin expected</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td><strong>Immunosuppressants</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyclosporine, Everolimus, Sirolimus, Tacrolimus</td>
<td>EFV, ETR, NVP</td>
<td>↓ immunosuppressant possible</td>
<td>Increase in immunosuppressant dose may be necessary. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with specialist as necessary.</td>
</tr>
<tr>
<td><strong>Narcotics/Treatments for Opioid Dependence</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buprenorphine Sublingual or buccal</td>
<td>EFV</td>
<td>Buprenorphine AUC ↓ 50%</td>
<td>No dose adjustment recommended; monitor for withdrawal symptoms.</td>
</tr>
<tr>
<td></td>
<td>ETR, NVP</td>
<td>↑ buprenorphine expected</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>EFV</td>
<td>Buprenorphine AUC ↓ 25%</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>No significant effect</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Methadone</td>
<td>EFV</td>
<td>Methadone AUC ↓ 52%</td>
<td>Opoid withdrawal common; increased methadone dose often necessary.</td>
</tr>
<tr>
<td></td>
<td>ETR, NVP</td>
<td>No significant effect</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Rilpivirine</td>
<td>NVP</td>
<td>Methadone AUC ↓ 37% to 51%</td>
<td>Opoid withdrawal common; increased methadone dose often necessary.</td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>R-methadone\textsuperscript{c} AUC ↓ 16%</td>
<td>No dose adjustment necessary, but monitor for withdrawal symptoms.</td>
</tr>
<tr>
<td><strong>PDE5 Inhibitors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sildenafil</td>
<td>ETR</td>
<td>Sildenafil AUC ↓ 57%</td>
<td>May need to increase sildenafil dose based on clinical effect.</td>
</tr>
<tr>
<td></td>
<td>EFV, NVP</td>
<td>↓ sildenafil possible</td>
<td>May need to increase PDE5 inhibitor dose based on clinical effect.</td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>← sildenafil</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Avanafil, Tadalafil, Vardenafil</td>
<td>EFV, ETR, NVP</td>
<td>↓ PDE5 inhibitor possible</td>
<td>May need to increase PDE5 inhibitor dose based on clinical effect.</td>
</tr>
</tbody>
</table>

\*Approved dose for RPV is 25 mg once daily. Most PK interaction studies were performed using 75 to 150 mg per dose.

\*b Norbuprenorphine is an active metabolite of buprenorphine.

\*c R-methadone is the active form of methadone.

**Key to Symbols:**

↑ = increase  
↓ = decrease  
← = no change

**Key to Acronyms:**  
ARV = antiretroviral; AUC = area under the curve; BID = twice daily; CCB = calcium channel blockers; C\textsubscript{max} = maximum plasma concentration; C\textsubscript{min} = minimum plasma concentration; DAA = direct-acting antivirals; DHA = dithroartemisin; DMPA = depot medroxyprogesterone acetate; EFV = efavirenz; ETR = etravirine; HMG-CoA = hydroxy-methylglutaryl-coenzyme A; INR = international normalized ratio; MAC = Mycobacterium avium complex; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; OH-itraconazole = active metabolite of itraconazole; PCP = Pneumocystis jiroveci pneumonia; PDE5 = phosphodiesterase type 5; PI = protease inhibitor; PIIr = protease inhibitor/ritonavir; PK = pharmacokinetic; PPI = proton pump inhibitor; RPV = rilpivirine; RTV = ritonavir

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV

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