# ART Drug-Drug Interactions

*Updated February 2021*

<table>
<thead>
<tr>
<th>Class or Drug</th>
<th>Mechanism of Action</th>
<th>Clinical Comments</th>
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</table>
| Proton pump inhibitors (PPIs) [Schafer and Short 2012] | • PPIs inhibit secretion of gastric acid by proton pumps thereby increasing gastric pH.  
• RPV requires an acidic environment for optimal absorption. | Avoid concomitant use (may decrease RPV absorption).                                |
| Histamine 2 antagonists (H2As) [Schafer and Short 2012] | • H2As inhibit secretion of gastric acid by proton pumps, thereby increasing gastric pH.  
• RPV requires an acidic environment for optimal absorption. | • Give H2A at least 12 hours before or 4 hours after RPV.  
• Concomitant use may decrease RPV absorption.  
• Use lowest effective dose.  
• Administer with food. |
| Antacids [Schafer and Short 2012]                  | • Antacids increase gastric pH.  
• RPV requires an acidic environment for optimal absorption.  
• Concomitant use may decrease RPV absorption. | • Give antacids 2 hours before or 4 hours after RPV.                                    |
| GLP-1 agonists                                    | Caution needed when coadministering with RPV and GLP-1 agonists, such as exenatide, due to their potential to inhibit gastric secretion, thereby reducing absorption of RPV.  
Furthermore, exenatide has the potential to slow gastric emptying. | Consider taking RPV 4 hours before exenatide.                                      |
| Dexamethasone [Welz, et al. 2017]                 | Dexamethasone is an inducer of CYP3A, which is primarily responsible for the metabolism of RPV. | **Systemic dexamethasone:** 1) Contraindicated; consider use of alternative agents. 2) If using more than single dose, do not coadminister. |
| Anti-arrhythmic drugs [Sanford 2012]              | Supratherapeutic doses of RPV have caused QT prolongation, and additive effects may be seen. | Avoid concomitant use (may cause QT prolongation and torsades de pointes).           |
| Long-acting beta agonists (LABAs)                 | RPV and drugs from the LABA class may both theoretically increase QT interval, especially at high doses. | • No dose adjustment necessary.  
• Do not use more LABA than recommended; this can increase risk of QT prolongation. |
### Table 9: Rilpivirine (RPV) Interactions (also see drug package inserts)

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<th>Class or Drug</th>
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<tbody>
<tr>
<td><strong>Antipsychotics</strong></td>
<td>No significant interactions noted.</td>
<td>No dose adjustments necessary, but avoid excess doses of either antipsychotic or RPV because excess doses of both drugs may increase risk of QT prolongation.</td>
</tr>
</tbody>
</table>
| **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. |
| **Methadone, buprenorphine (BUP)** | • **BUP**: No significant interactions are expected.  
• **Methadone**: Mildly reduces methadone concentrations. | • **Methadone**: Monitor for signs of methadone withdrawal and increase dose as necessary.  
• Use methadone or BUP cautiously with RPV because supratherapeutic doses of RPV have been known to cause increase in QT prolongation. |
| **Strong inducers or inhibitors of CYP3A** | RPV is a substrate of CYP3A, and as such, drugs that affect its metabolism affect its concentrations. | • Avoid concomitant use if possible.  
• Dose adjustments of RPV are not recommended.  
• Consider alternative concomitant agents. |

**Abbreviations**: ARV, antiretroviral; BUP, buprenorphine; CYP, cytochrome P450;  
**No significant interactions/no dose adjustments necessary**: Common oral antibiotics (Table 15); drugs used as antihypertensive agents (Table 16); anticoagulants (Table 17); antiplatelet drugs (Table 18); statins (Table 19); asthma and allergy medications (Table 23); antidepressants (Table 26); benzodiazepines (Table 27); sleep medications (Table 28); anticonvulsants not specifically stated above (Table 30); non-opioid pain medications (Table 31); opioid analgesics and tramadol (Table 32); erectile and sexual dysfunction agents (Table 34); tobacco and smoking cessation products (Table 35); alcohol, disulfiram, and acamprosate (Table 36); naloxone and naltrexone (Table 37); immunosuppressants (Table 38); gender-affirming hormones (Table 40).