ART Drug-Drug Interactions

Updated February 2021

Table 9: Rilpivirine (RPV) Interactions (also see drug package inserts)

Class or Drug	Mechanism of Action	Clinical Comments
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)		
Class or Drug	**Mechanism of Action**	**Clinical Comments**
Antipsychotics	No significant interactions noted.	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.
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).