Resource: ART Drug-Drug Interactions

August 2024

Table 9: Raltegravir (RAL) Interactions (also see drug package inserts)

Class or Drug	Mechanism of Action	Clinical Comments
Antacids and other polyvalent cations [Krishna, et al. 2016; Calcagno, et al. 2015; Kiser, et al. 2010]	RAL chelates with cations, forming insoluble compounds that inactivate both drugs.	• **Aluminum-magnesium hydroxide antacids:** Concomitant use is contraindicated; use alternative acid-reducing agent. • **Calcium carbonate antacids:** – RAL HD once per day is *contraindicated.* – RAL 400 mg twice per day: No dose adjustment or separation is necessary. • **Other polyvalent cations:** Administer at least 2 hours before or 6 hours after.
Anticonvulsants	Coadministration with strong UGT1A1 inducers (phenytoin, phenobarbital, etc.) may decrease RAL concentrations.	Coadministration with strong UGT1A1 inducers is not recommended.
Rifabutin, rifampin, rifapentine	• **Rifabutin:** No clinically significant interactions are expected. • **Rifampin:** CYP3A4 induction reduces RAL bioavailability. • **Rifapentine:** Induction of metabolism may reduce RAL metabolism.	• **Rifabutin:** No dose adjustments are necessary. • **Rifampin:** – When used concomitantly, dose RAL at 800 mg twice per day instead of 400 mg twice per day. – Do not use RAL HD. • **Rifapentine:** – For 900 mg once-weekly rifapentine and RAL 400 mg twice daily, no dose adjustments are necessary. – Do not coadminister RAL with once-daily rifapentine.

Abbreviations: CYP, cytochrome P450; UGT, uridine diphosphate glucuronosyltransferase.

No significant interactions/no dose adjustments necessary (see guideline section Drug-Drug Interactions by Common Medication Class)**:** Common oral antibiotics; antihypertensive medications; anticoagulants; antiplatelet medications; statins; antidiabetic medications; acid-reducing agents; asthma and allergy medications; long-acting beta agonists; inhaled and injected corticosteroids; antidepressants; benzodiazepines; sleep medications; antipsychotics; nonopioid pain medications; opioid analgesics and tramadol; hormonal contraceptives; erectile and sexual dysfunction agents; alpha-adrenergic antagonists for benign prostatic hyperplasia; tobacco and smoking cessation products; alcohol, disulfiram, and acamprosate; methadone, buprenorphine, naloxone, and naltrexone; immunosuppressants; COVID-19 therapeutics; mpox treatments; gender-affirming hormones; ADHD medications and lithium.

References

Calcagno A, D'Avolio A, Bonora S. Pharmacokinetic and pharmacodynamic evaluation of raltegravir and experience from clinical trials in HIV-positive patients. *Expert Opin Drug Metab Toxicol* 2015;11(7):1167-76. [PMID: 26073580] https://pubmed.ncbi.nlm.nih.gov/26073580

Kiser JJ, Bumpass JB, Meditz AL, et al. Effect of antacids on the pharmacokinetics of raltegravir in human immunodeficiency virus-seronegative volunteers. *Antimicrob Agents Chemother* 2010;54(12):4999-5003. [PMID: 20921313] https://pubmed.ncbi.nlm.nih.gov/20921313

Krishna R, East L, Larson P, et al. Effect of metal-cation antacids on the pharmacokinetics of 1200 mg raltegravir. *J Pharm Pharmacol* 2016;68(11):1359-65. [PMID: 27671833] https://pubmed.ncbi.nlm.nih.gov/27671833