

## Interactions between Acid-Reducing Agents and Antiretrovirals

|                             | Antacids, Vitamins, etc.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | H2 Antagonists (H2RA)                                                                                                                                                                                                                                                                  | Proton Pump Inhibitors (PPIs)                                                                                                                                              |
|-----------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | <i>*equivalent doses:</i><br><u>H2RAs (treatment):</u><br>Famotidine 20 mg BID or 40 mg qhs<br>Nizatidine 150 mg BID or 300 mg qhs<br>Ranitidine 150 mg BID or 300 mg qhs<br><br><u>H2RAs (maintenance):</u><br>Famotidine 20 mg qhs<br>Nizatidine 150 mg qhs<br>Ranitidine 150 mg qhs | <i>*equivalent doses:</i><br><u>PPIs (daily standard dose):</u><br>Esomeprazole 20 mg<br>Lansoprazole 30 mg<br>Omeprazole 20 mg<br>Pantoprazole 40 mg<br>Rabeprazole 20 mg |
| <b>Integrase Inhibitors</b> |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                        |                                                                                                                                                                            |
| Dolutegravir                | <b>Antacids:</b> <ul style="list-style-type: none"> <li>Dolutegravir AUC ↓ 74% with simultaneous administration, ↓ 26% with staggered administration<sup>1</sup></li> </ul> <p>Calcium carbonate 1200 mg or ferrous fumarate 324 mg:</p> <ul style="list-style-type: none"> <li>Dolutegravir exposures comparable to dolutegravir given alone if co-administered under fed conditions.</li> <li>Dolutegravir exposures ↓ 37-39% with calcium and ↓ 54-57% with iron, if co-administered in the fasted state.<sup>2, 3</sup></li> </ul> <p>Dolutegravir should be administered 2 hours before or 6 hours after medications containing polyvalent cations (e.g., Mg, Al, Fe, or Ca) including cation-containing antacids or laxatives, sucralfate, oral iron or calcium supplements, and buffered medications. If taken with food, dolutegravir may be taken at the same time as calcium or iron supplements.<sup>2</sup></p> | Dolutegravir may be co-administered with H2-antagonists without dose adjustment. <sup>1</sup>                                                                                                                                                                                          | Dolutegravir may be co-administered with PPIs without dose adjustment. <sup>1</sup>                                                                                        |

|              | Antacids, Vitamins, etc.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | H2 Antagonists (H2RA)                                                                                                                                                                                                                                                                  | Proton Pump Inhibitors (PPIs)                                                                                                                                              |
|--------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | <i>*equivalent doses:</i><br><u>H2RAs (treatment):</u><br>Famotidine 20 mg BID or 40 mg qhs<br>Nizatidine 150 mg BID or 300 mg qhs<br>Ranitidine 150 mg BID or 300 mg qhs<br><br><u>H2RAs (maintenance):</u><br>Famotidine 20 mg qhs<br>Nizatidine 150 mg qhs<br>Ranitidine 150 mg qhs | <i>*equivalent doses:</i><br><u>PPIs (daily standard dose):</u><br>Esomeprazole 20 mg<br>Lansoprazole 30 mg<br>Omeprazole 20 mg<br>Pantoprazole 40 mg<br>Rabeprazole 20 mg |
|              | Multivitamin (containing 162 mg elemental calcium, 100 mg manganium): <sup>1</sup> <ul style="list-style-type: none"> <li>dolutegravir AUC ↓ 33%</li> </ul> Dolutegravir can be administered without regard to multivitamins.                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                        |                                                                                                                                                                            |
| Elvitegravir | Elvitegravir AUC ↓ 45%, Cmin ↓ 41% with simultaneous antacid administration (20 mL); no change in elvitegravir exposures with staggered antacid administration.<br><br>Elvitegravir should be separated by at least 2 hours from antacids containing aluminum, magnesium hydroxide, or calcium carbonate. <sup>4</sup>                                                                                                                                                                                                                                                                 | Elvitegravir/cobicistat may be given with H2-blockers without dosage adjustment. <sup>5</sup>                                                                                                                                                                                          | Elvitegravir/cobicistat may be given with PPIs without dosage adjustment. <sup>5</sup>                                                                                     |
| Raltegravir  | Raltegravir AUC ↓ 49%, Cmin ↓ 63% with simultaneous aluminum/magnesium antacid (20 mL) administration. <sup>6</sup> Taking an aluminum and magnesium antacid within 6 hours of raltegravir administration also significantly decreased raltegravir plasma levels (50% ↓ Cmin. Manufacturer states that concomitant or staggered administration of antacids containing aluminium and/or magnesium is not recommended. <sup>7</sup><br><br>When calcium carbonate antacid was administered 2 hours prior to raltegravir, raltegravir Cmin ↓ 32%, but this interaction was not considered | Raltegravir may be coadministered with famotidine without dose adjustment. <sup>8</sup>                                                                                                                                                                                                | Raltegravir may be coadministered with omeprazole without dose adjustment. <sup>9</sup>                                                                                    |

|               | Antacids, Vitamins, etc.                                                                                          | H2 Antagonists (H2RA)                                                                                                                                                                                                                                                                                                                                                                                                                                        | Proton Pump Inhibitors (PPIs)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
|---------------|-------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|               |                                                                                                                   | <p><i>*equivalent doses:</i><br/> <u>H2RAs (treatment):</u><br/> Famotidine 20 mg BID or 40 mg qhs<br/> Nizatidine 150 mg BID or 300 mg qhs<br/> Ranitidine 150 mg BID or 300 mg qhs</p> <p><u>H2RAs (maintenance):</u><br/> Famotidine 20 mg qhs<br/> Nizatidine 150 mg qhs<br/> Ranitidine 150 mg qhs</p>                                                                                                                                                  | <p><i>*equivalent doses:</i><br/> <u>PPIs (daily standard dose):</u><br/> Esomeprazole 20 mg<br/> Lansoprazole 30 mg<br/> Omeprazole 20 mg<br/> Pantoprazole 40 mg<br/> Rabeprazole 20 mg</p>                                                                                                                                                                                                                                                                                                                                                 |
|               | clinically meaningful. <sup>7</sup> May give raltegravir with antacids containing calcium carbonate. <sup>7</sup> |                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| <b>NNRTIs</b> |                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| Rilpivirine   | Administer antacids at least 2 hours before or at least 4 hours after rilpivirine. <sup>10</sup>                  | Rilpivirine AUC ↓ 76% with famotidine 40 mg. Rilpivirine should be separated at least 4 hours before or 12 hours following famotidine. <sup>11</sup>                                                                                                                                                                                                                                                                                                         | 37% ↓ Cmin of rilpivirine with omeprazole 20 mg. <b>Rilpivirine is contraindicated with PPIs.</b> <sup>10</sup>                                                                                                                                                                                                                                                                                                                                                                                                                               |
| <b>PIs</b>    |                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| Atazanavir    | Administer antacids 1 hour before or 2 hours after atazanavir. <sup>12</sup>                                      | <p><u>Famotidine:</u></p> <ul style="list-style-type: none"> <li>41% ↓ AUC and 42% ↓ Cmin of atazanavir (unboosted)<sup>13</sup></li> <li>20-23% ↓ AUC, Cmin of atazanavir (boosted)<sup>14</sup></li> </ul> <p>Give ATV 300/100 mg QD with famotidine simultaneously or 10 hours after H2RA. Maximum famotidine 40 mg BID (treatment-naïve) or 20 mg BID (treatment-experienced). If also on tenofovir, ↑ to ATV 400/100 mg QD in experienced patients.</p> | <p>Omeprazole 40 mg:</p> <ul style="list-style-type: none"> <li>93% ↓ atazanavir Cmin (unboosted),<sup>15</sup></li> <li>78% ↓ atazanavir Cmin (boosted)<sup>16</sup></li> </ul> <p>Omeprazole 20 mg:</p> <ul style="list-style-type: none"> <li>27% ↓ atazanavir Cmin (boosted)<sup>17</sup></li> </ul> <p>Coadministration of atazanavir with PPIs is not recommended. If coadministration is unavoidable, ↑ to atazanavir 400/100 mg and do not exceed omeprazole 20 mg.<sup>12</sup> Recommend close monitoring and TDM if available.</p> |

# References:

1. Patel P, Song I, Borland J, et al. Pharmacokinetics of the HIV integrase inhibitor S/GSK1349572 co-administered with acid-reducing agents and multivitamins in healthy volunteers. J Antimicrob Chemother 2011;66(7):1567-72.
2. ViiV Healthcare ULC. Tivicay (dolutegravir) Prescribing Information. Laval, QC February 26, 2014.
3. Song I, Borland J, Arya N, et al. The effect of calcium and iron supplements on the pharmacokinetics of dolutegravir in healthy subjects [abstract P\_13]. 15th International Workshop on Clinical Pharmacology of HIV and Hepatitis Therapy, May 19-21, 2014, Washington, DC.
4. Gilead Sciences Canada Inc. Stribild (elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil fumarate) Product Monograph. Mississauga, ON February 6, 2014.
5. Ramanathan S, Mathias A, Wei X, et al. Pharmacokinetics of once-daily boosted-elvitegravir when administered in combination with acid reducing agents. J Acq Immune Def Syndr 2013;64(1):45-50.
6. Kiser JJ, Bumpass JB, Meditz A, et al. Effect of antacids on the pharmacokinetics of raltegravir in human immunodeficiency virus-seronegative volunteers. Antimicrob Agents Chemother 2010;54(12):4999-5003.
7. Merck Frosst Canada Ltd. Isentress (raltegravir) Prescribing Information. Kirkland, QC January 20, 2015.
8. Rhame F, Matson M, Wood D, et al. Effects of famotidine and omeprazole on raltegravir pharmacokinetics in HIV-infected individuals [abstract PE4.1/1]. 12th European AIDS Conference, November 11-14, 2009, Cologne, Germany.
9. Iwamoto M, Wenning L, Nguyen BY, et al. Effects of omeprazole on plasma levels of raltegravir. Clin Infect Dis 2009;48(4):489-92.
10. Janssen Inc. Edurant (rilpivirine) Product Monograph. Titusville, NJ May, 2014.
11. Van Heeswijk RP, Hoetelmans RM, Kestens D, et al. The pharmacokinetic (PK) interaction between famotidine and TMC278, a next generation non-nucleoside reverse transcriptase inhibitor (NNRTI), in HIV-negative volunteers [abstract TUPDB01]. 4th International AIDS Society Conference on HIV Pathogenesis, Treatment and Prevention, July 22-25 2007, Sydney, Australia.
12. Bristol-Myers Squibb Canada. Reyataz (atazanavir) Product Monograph. Montreal, QC July 4, 2013.
13. Agarwala S. Pharmacokinetic effect of famotidine on atazanavir with and without ritonavir in healthy subjects [abstract 11]. 6th International Workshop on Clinical Pharmacology of HIV Therapy, April 28-30, 2005, Quebec City, Canada.
14. Wang X, Boffito M, Zhang J, et al. Effects of the H2-receptor antagonist famotidine on the pharmacokinetics of atazanavir-ritonavir with or without tenofovir in HIV-infected patients. AIDS Patient Care STDS 2011;25(9):509-15.
15. Agarwala S, Gray K, Eley T, et al. Pharmacokinetic interaction between atazanavir and omeprazole in healthy subjects [poster WePe3.3C08]. 3rd International AIDS Society Conference on HIV Pathogenesis and Treatment, July 24-27, 2005, Rio de Janeiro.

16. Agarwala S, Gray K, Wang Y, et al. Pharmacokinetic effect of omeprazole on atazanavir with ritonavir in healthy subjects [abstract 658]. 12th Conference on Retroviruses and Opportunistic Infections, February 22-25, 2005, Boston.
17. Lubner A, Brower R, Kim D, et al. Steady-state pharmacokinetics of once-daily fosamprenavir/ritonavir and atazanavir/ritonavir alone and in combination with 20 mg omeprazole in healthy volunteers. HIV Medicine 2007;8(7):457-64.