



Resource: ART Drug-Drug Interactions

April 2023

Table 26: Polyvalent Cations (also see drug package inserts)		
→ Supplements, antacids, and laxatives that contain aluminum, calcium, magnesium, zinc, and iron		
Class or Drug	Mechanism of Action	Clinical Comments
<ul style="list-style-type: none"> • NRTIs • Darunavir (DRV), boosted or unboosted • Efavirenz (EFV) • Etravirine (ETR) • Doravirine (DOR) • Fostemsavir (FTR) 	No clinically significant interactions reported.	No dose adjustments are necessary.
All INSTIs	INSTIs form complexes with cations, resulting in reduced concentrations of both INSTIs and cations. For specific recommendations, see individual INSTIs below.	Any polyvalent cation: If coadministration is necessary, administer at least 2 hours before or at least 6 hours after; monitor for virologic efficacy.
Dolutegravir (DTG)	DTG chelates with cations, forming insoluble compounds that inactivate both drugs.	<ul style="list-style-type: none"> • Divalent and trivalent cations (aluminum, magnesium, calcium, zinc, etc.): Administer DTG 2 hours before or 6 hours after. • Calcium- and iron-containing supplements: DTG and supplement may be used concomitantly if taken with food. • Iron salts: <ul style="list-style-type: none"> – Administer DTG 2 hours before or 6 hours after. – DTG and iron salts may be used concomitantly if taken with food.
Bictegravir (BIC)	BIC can chelate with cations, reducing absorption of both drugs.	<ul style="list-style-type: none"> • Aluminum/magnesium-containing antacids: Administer at least 6 hours before or 2 hours after BIC. • Calcium-containing antacids: <ul style="list-style-type: none"> – Administer BIC and antacids together with food. – Do not coadminister BIC simultaneously with antacids on empty stomach. • Calcium- or iron-containing supplements: <ul style="list-style-type: none"> – If taken with food, BIC can be taken at same time. – If not taken with food, these supplements should be administered as with antacids.

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→ Supplements, antacids, and laxatives that contain aluminum, calcium, magnesium, zinc, and iron

Class or Drug	Mechanism of Action	Clinical Comments
Elvitegravir (EVG), boosted	EVG chelates with polyvalent cations, which may reduce absorption of both agents.	<ul style="list-style-type: none"> • Aluminum-, magnesium-, and/or calcium-containing antacids: When taken with EVG, separate doses by at least 2 hours. • Other polyvalent cations: Administer at least 2 hours before or 6 hours after EVG.
Raltegravir (RAL)	RAL chelates with cations, forming insoluble compounds that inactivate both drugs.	<ul style="list-style-type: none"> • Aluminum-magnesium hydroxide antacids: Concomitant use is contraindicated; use alternative acid-reducing agent. • Calcium carbonate antacids: <ul style="list-style-type: none"> – RAL HD once per day is <i>contraindicated</i>. – 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.
Atazanavir (ATV), boosted or unboosted	Antacids: ATV requires acidic gastric pH for absorption; acid-reducing agents interfere with ATV absorption.	Antacids or buffered medications: Administer ATV at least 2 hours before or 1 to 2 hours after.
Cabotegravir (CAB)	Antacids containing polyvalent cations (i.e., aluminum or magnesium hydroxide, calcium carbonate): Antacids increase gastric pH, and CAB requires acidic environment for optimal absorption. Concomitant use may decrease CAB absorption.	Antacids containing polyvalent cations (i.e., aluminum or magnesium hydroxide, calcium carbonate): <ul style="list-style-type: none"> • Administer antacid products at least 2 hours before or 4 hours after <i>oral</i> CAB. • No effect of antacid use is expected on <i>injectable</i> CAB.
Rilpivirine (RPV)	Antacids: <ul style="list-style-type: none"> • Antacids increase gastric pH. • RPV requires acidic environment for optimal absorption. • Concomitant use may decrease RPV absorption. 	Antacids: Administer antacids 2 hours before or 4 hours after.
Abbreviations: ARV, antiretroviral; INSTI, integrase strand transfer inhibitor; NRTI, nucleoside reverse transcriptase inhibitor.		