



Resource: ART Drug-Drug Interactions

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Table 32: Benzodiazepines [a] (also see drug package inserts)		
Class or Drug	Mechanism of Action	Clinical Comments
<ul style="list-style-type: none"> • NRTIs • Dolutegravir (DTG) • Bictegravir (BIC) • Cabotegravir (CAB) • Raltegravir (RAL) • Rilpivirine (RPV) • Doravirine (DOR) • Fostemsavir (FTR) 	No significant interactions reported.	No dose adjustments are necessary.
Elvitegravir (EVG), boosted	<ul style="list-style-type: none"> • Boosting with cobicistat: May increase benzodiazepine concentrations via CYP3A4 inhibition. • Midazolam, triazolam: Levels likely to be increased by COBI-boosted EVG 	<ul style="list-style-type: none"> • Alprazolam, clonazepam, diazepam: Consider alternative benzodiazepine (e.g., lorazepam, oxazepam, temazepam); if used, administer lowest effective dose; monitor closely for adverse effects. • Midazolam: <ul style="list-style-type: none"> – Oral: Concomitant use is contraindicated. – Parenteral: Administer in closely monitored setting. Consider dose reduction, especially if >1 dose is administered. • Triazolam: Concomitant use is contraindicated.
Boosted PIs	<ul style="list-style-type: none"> • Alprazolam: Boosted ARVs may increase alprazolam concentrations via CYP3A4 inhibition. • Diazepam: CYP3A4 inhibition may reduce metabolism of diazepam. 	<ul style="list-style-type: none"> • Consider alternative benzodiazepine (e.g., lorazepam, oxazepam, temazepam). If used, administer lowest effective dose; monitor closely for adverse effects. • Diazepam: Monitor for excess sedation.
Efavirenz (EFV)	Alprazolam, diazepam: EFV may reduce alprazolam and diazepam concentrations.	<ul style="list-style-type: none"> • Alprazolam: Monitor for benzodiazepine withdrawal if patient starts taking EFV. • Alprazolam, clonazepam, diazepam: Titrate slowly to achieve clinical effect; monitor for benzodiazepine efficacy.
Etravirine (ETR)	Alprazolam, diazepam: ETR may reduce alprazolam and diazepam concentrations.	Alprazolam: Monitor for benzodiazepine withdrawal.
Lenacapavir (LEN)	Midazolam (oral), triazolam: Moderate inhibition of CYP3A4 and P-gP potentially increases sedative levels.	Midazolam (oral), triazolam: Use with caution; monitor for excess sedation.
<p>Abbreviations: ARV, antiretroviral; COBI, cobicistat; CYP, cytochrome P450; NRTI, nucleoside reverse transcriptase inhibitor; P-gP, P-glycoprotein; PI, protease inhibitor.</p> <p>Note:</p> <p>a. Lorazepam, oxazepam, and temazepam do not interact clinically with and do not require dose adjustments when coadministered with ARVs.</p>		