ART Drug-Drug Interactions: Dolutegravir (DTG) Interactions

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Table 7: Dolutegravir (DTG) Interactions (also see drug package inserts)		
Class or Drug	**Mechanism of Action**	**Clinical Comments**
Dofetilide [Feng and Varma 2016; Max and Vibhakar 2014]	DTG inhibits renal OCT2 and MATE1, and these transporters eliminate dofetilide.	Avoid concomitant use (may cause QT prolongation or torsades de pointes).
Metformin [Gervasoni, et al. 2017; Song, et al. 2016]	DTG inhibits renal OCT2, MATE1, and MATE2, which are involved in metformin elimination.	• Administer at lowest dose possible to achieve glycemic control; monitor for adverse effects. • Titrate to achieve clinical effect but do not exceed 1,000 mg daily; monitor for adverse effects, including lactic acidosis.
Divalent and trivalent cations (aluminum, magnesium, calcium, zinc, etc.) [Song, et al. 2015; Cottrell, et al. 2013]	DTG chelates with cations forming insoluble compounds that inactivate both drugs.	• 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 [Song, et al. 2015]	DTG chelates with cations, forming insoluble compounds that inactivate both drugs.	• Administer DTG 2 hours before or 6 hours after. • DTG and iron salts may be used concomitantly if taken with food.
Atenolol	Atenolol is eliminated via OCT2 and MATE1, which are inhibited by DTG. Coadministration may increase atenolol levels.	• Start at lower atenolol dose and titrate slowly to achieve clinical effect. • If patient is already using atenolol but starting DTG, monitor for atenolol-related adverse effects. • Reduce atenolol dose if necessary or switch to another ARV.
Etravirine (ETR) [Green, et al. 2017]	• ETR induces UGT1A1 and CYP3A enzymes. • DTG is a substrate of UGT1A1 and CYP3A enzymes.	• ETR reduces DTG concentrations. Do not use concomitantly unless boosted PI is also part of treatment regimen.
Rifabutin, rifampin, rifapentine	• **Rifabutin:** No clinically significant interactions are expected. • **Rifampin:** CYP3A induction reduces DTG bioavailability. • **Rifapentine:** Reduced rifapentine levels are expected.	• **Rifabutin:** No dose adjustments are necessary. • **Rifampin:** When used concomitantly, administer DTG at 50 mg twice per day instead of 50 mg once per day in patients without suspected or documented INSTI-associated resistance mutations. Consider rifabutin in patients with INSTI resistance. • **Rifapentine, once weekly:** – If using concomitant DTG 50 mg once daily, monitor for virologic efficacy. – Do not coadminister with DTG 50 mg twice daily. • **Rifapentine, once daily:** Do not coadminister DTG.

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Abbreviations: ARV, antiretroviral; CYP, cytochrome P450; INSTI, integrase strand transfer inhibitor; MATE, multidrug and toxin extrusion; OCT, organic cation transporter.		
No significant interactions/no dose adjustments necessary: Common oral antibiotics (Table 19); anticoagulants (Table 21); antiplatelet drugs (Table 22); statins (Table 23); acid-reducing agents (Table 25); asthma and allergy medications (Table 27); long-acting beta agonists (Table 28); inhaled and injected corticosteroids (Table 29); antidepressants (Table 30); benzodiazepines (Table 31); sleep medications (Table 32); antipsychotics (Table 33); nonopioid pain medications (Table 35); opioid analgesics and tramadol (Table 36); hormonal contraceptives (Table 37); erectile and sexual dysfunction agents (Table 38); alpha-adrenergic antagonists for benign prostatic hyperplasia (Table 39); tobacco and smoking cessation products (Table 40); alcohol, disulfiram, and acamprosate (Table 41); methadone, buprenorphine, naloxone, and naltrexone (Table 42); immunosuppressants (Table 43); COVID-19 therapeutics (Table 45); mpox treatments (Table 46); gender-affirming hormones (Table 47).		

References

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