ART Drug-Drug Interactions

Updated February 2021

Table 5: Dolutegravir (DTG) Interactions (also see drug package inserts)		
Class or Drug	**Mechanism of Action**	**Clinical Comments**
Dofetilide [Max and Vibhakar 2014; Feng and Varma 2016]	DTG inhibits renal OCT2 and MATE1, and these transporters eliminate dofetilide.	Avoid concomitant use (may cause QT prolongation or torsade de pointes).
Metformin [Song, et al. 2016; Gervasoni, et al. 2017]	DTG inhibits renal OCT2, MATE1, and MATE2, which are involved in elimination of metformin.	• Administer at lowest dose possible to achieve glycemic control; monitor for adverse effects. • Titrate metformin and do not exceed 1,000 mg daily when coadministered with DTG; monitor for adverse effects, including lactic acidosis.
Pioglitazone [Fantauzzi, et al. 2013]	Pioglitazone is a weak inducer of CYP3A, and DTG is partially metabolized by this enzyme.	Avoid concomitant use because this may decrease DTG concentrations.
Divalent and trivalent cations (aluminum, magnesium, calcium, zinc, etc.) [Cottrell, et al. 2013; Song, et al. 2015]	DTG chelates with cations forming insoluble compounds that inactivate both drugs.	• Administer DTG 2 hours before or 6 hours after taking cations. • Calcium-containing supplements 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 taking iron salts. • These drugs may be used concomitantly if taken with food.
Atenolol	• Atenolol is eliminated via OCT2 and MATE1, which are inhibited by DTG. Coadministration may increase levels of atenolol.	• Start at a lower dose of atenolol and adjust slowly until desired clinical effect is achieved. • If patient is already on atenolol but starting DTG, monitor for atenolol-related adverse events. • Reduce dose of atenolol if necessary or switch to another ARV agent.
Rifabutin, rifampin	• **Rifabutin:** No clinically significant interactions. • **Rifampin** induction of CYP3A reduces bioavailability of DTG.	**Rifampin:** When used concomitantly, dose DTG at 50 mg twice per day instead of 50 mg once per day.

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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 15); anticoagulants (Table 17); antiplatelet drugs (Table 18); statins (Table 19); acid-reducing agents (Table 21); asthma and allergy medications (Table 23); long-acting beta agonists (Table 24); inhaled and injected corticosteroids (Table 25); antidepressants (Table 26); benzodiazepines (Table 27); sleep medications (Table 28); antipsychotics (Table 28); non-opioid pain medications (Table 31); opioid analgesics and tramadol (Table 32); hormonal contraceptives (Table 33); erectile and sexual dysfunction agents (Table 34); tobacco and smoking cessation products (Table 35); alcohol, disulfiram, and acamprosate (Table 36); methadone, buprenorphine, naloxone, and naltrexone (Table 37); immunosuppressants (Table 38); gender-affirming hormones (Table 40).		