ART Drug-Drug Interactions

*July 2021*

**Table 5: Dolutegravir (DTG) Interactions** *(also see drug package inserts)*

<table>
<thead>
<tr>
<th>Class or Drug</th>
<th>Mechanism of Action</th>
<th>Clinical Comments</th>
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<tbody>
<tr>
<td>Dofetilide</td>
<td>DTG inhibits renal OCT2 and MATE1, and these transporters eliminate dofetilide.</td>
<td>Avoid concomitant use (may cause QT prolongation or torsade de pointes).</td>
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</table>
| Metformin     | 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  | 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.) | 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    | 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, rifapentine | • **Rifabutin:** No clinically significant interactions.  
• **Rifampin, rifapentine:** Induction of CYP3A reduces bioavailability of DTG. | • **Rifabutin:** Use standard doses  
• **Rifampin:** When used concomitantly, dose 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:** Do not coadminister. |
Table 5: Dolutegravir (DTG) Interactions (also see drug package inserts)

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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); nonopioid 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).  
References  