### ART Drug-Drug Interactions: Antipsychotics

**April 2023**

<table>
<thead>
<tr>
<th>Class or Drug</th>
<th>Mechanism of Action</th>
<th>Clinical Comments</th>
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</thead>
<tbody>
<tr>
<td>NRTIs, Dolutegravir (DTG), Bictegravir (BIC), Cabotegravir (CAB), Raltegravir (RAL), Doravirine (DOR)</td>
<td>No significant interactions are expected.</td>
<td>No dose adjustments are necessary.</td>
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</table>
| Elvitegravir (EVG), boosted | Several antipsychotic agents are substrates of CYP3A, and inhibitors of this enzyme may increase their concentrations. | **Quetiapine**: Reduce dose to 1/6 if initiating ART in patients on stabilized quetiapine.  
**All other antipsychotics**: Use at lowest dose possible in patients taking boosted ARVs; monitor for adverse effects. |
| Elvitegravir (EVG), boosted | **Haloperidol**: Boosted PIs may moderately increase haloperidol concentrations.  
**Aripiprazole, brexpiprazole**: RTV-boosted PIs may increase aripiprazole and brexpiprazole levels.  
**Risperidone**: Boosted PIs may moderately increase risperidone levels.  
**Clozapine**: Interaction has not been studied but boosted PIs may theoretically increase clozapine concentrations, increasing risk of adverse effects.  
**Iloperidone, lumateperone, lurasidone, cariprazine**: Levels are likely to be increased by all PIs, whether boosted or not. | **Quetiapine**:  
- Patients on stabilized quetiapine: Reduce dose to 1/6 if initiating ART; monitor for QT prolongation.  
- Patients stabilized on boosted PI: Use lowest dose and titrate slowly to achieve clinical effect; monitor for QT prolongation.  
**Lurasidone**: No data available. Avoid coadministration; consider alternative antipsychotic or ARV agent.  
**Haloperidol**: Monitor for QT prolongation.  
**Iloperidone**: Decrease iloperidone dose by 50%.  
**Aripiprazole**: Initiate at 25% of standard starting dose and titrate slowly to achieve clinical effect; monitor carefully for efficacy and adjust dose as necessary.  
**Brexiprazole**: Administer at 50% of brexiprazole dose and adjust dose as necessary.  
**Lumateperone**: Do not coadminister.  
**Pimozide**: Concomitant use is contraindicated.  
**Risperidone**: Initiate at low dose and titrate slowly to achieve clinical effect; monitor for adverse effects.  
**Ziprasidone**: Monitor for adverse effects, including QTc prolongation.  
**Cariprazine**: Consult DHHS guideline for full dosing recommendations and clinical comments [DHHS(c) 2021].  
**Clozapine**: Monitor carefully for clozapine-related adverse effects. |
Table 33: Antipsychotics [a] (also see drug package inserts)

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| Ritonavir (RTV)       | • **Haloperidol**: Boosted PIs may moderately increase haloperidol concentrations.    | • **Quetiapine**:  
  - Patients on stabilized quetiapine: If initiating ART, reduce dose to 1/6; monitor for QT prolongation.  
  - Patients stabilized on boosted PI: Use lowest dose and titrate slowly to achieve clinical effect; monitor for QT prolongation.  
  
  • **Aripiprazole, brexpiprazole**: RTV-boosted PIs may increase aripiprazole and brexpiprazole levels.  
  • **Risperidone**: Boosted PIs may moderately increase risperidone levels.  
  • **Clozapine**: Interaction has not been studied but RTV may theoretically increase clozapine concentrations, increasing risk of adverse effects.  
  • **Iloperidone, lumateperone, lurasidone, cariprazine**: Levels are likely to be increased by all PIs, whether boosted or not.  

• **Haloperidol**: Monitor for QT prolongation.  
• **Iloperidone**: Decrease iloperidone dose by 50%.  
• **Aripiprazole**: Initiate at 25% of standard starting dose and titrate slowly to achieve clinical effect; monitor carefully and adjust dose as necessary.  
• **Brexpiprazole**: Administer at 50% of brexpiprazole dose and adjust dose as necessary.  
• **Lumateperone**: Do not coadminister.  
• **Pimozide**: Concomitant use is contraindicated.  
• **Risperidone**: Initiate at low dose and titrate slowly to achieve clinical effect; monitor for adverse effects.  
• **Ziprasidone**: Monitor for adverse effects, including QTc prolongation.  
• **Cariprazine**: Consult DHHS guideline [DHHS(c) 2021] for full dosing recommendations and clinical comments [DHHS(c) 2021].  
• **Clozapine**: Monitor carefully for clozapine-related adverse effects.  
| Atazanavir (ATV), unboosted | **Lurasidone**: ATV decreases lurasidone metabolism via CYP3A.  | **Lurasidone**: Decrease lurasidone dose by 50%; monitor for adverse effects, including QT prolongation.  
• **Quetiapine**: EFV may reduce quetiapine concentrations.  
• **Aripiprazole, brexpiprazole**: EFV may decrease aripiprazole and brexpiprazole concentrations.  
• **Risperidone, olanzapine**: EFV may decrease risperidone and olanzapine efficacy.  
| Rilpivirine (RPV)       | No significant interactions reported.                                                | No dose adjustments are necessary, but avoid excess doses of either antipsychotic or RPV because excess doses of both drugs may increase risk of QT prolongation.  
| Efavirenz (EFV)         | • **Quetiapine**: EFV may reduce quetiapine concentrations.  | **Quetiapine, aripiprazole, brexpiprazole, risperidone, olanzapine**: Titrate slowly to achieve clinical effect; monitor for efficacy and adverse effects.  
• **Aripiprazole, brexpiprazole**: EFV may decrease aripiprazole and brexpiprazole concentrations.  
• **Risperidone, olanzapine**: EFV may decrease risperidone and olanzapine efficacy.  |
### Table 33: Antipsychotics [a] (also see drug package inserts)

First-generation, second-generation, atypical

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| Etravirine (ETR) | • Aripiprazole, brexpiprazole: ETR may decrease aripiprazole and brexpiprazole concentrations.  
• Risperidone: ETR may decrease risperidone efficacy. | Aripiprazole, brexpiprazole, risperidone: Titrate slowly to achieve clinical effect; monitor for efficacy and adverse effects. |
| Fostemsavir (FTR) | FTR may prolong QT. | Use caution when combining FTR with other medications known to prolong QT interval. |
| Lenacapavir (LEN) | Pimozide: Moderate inhibition of P-gP potentially increases pimozide levels. | Pimozide: Do not coadminister. |

**Abbreviations:** ART, antiretroviral therapy; ARV, antiretroviral; CYP, cytochrome P450; DHHS, U.S. Department of Health and Human Services; NRTI, nucleoside reverse transcriptase inhibitor; P-gP, P-glycoprotein; PI, protease inhibitor.

**Note:**
- Coadministration of antipsychotics and ARVs may result in QT prolongation; monitor closely.

### Reference