Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents
## Guidelines Development Process

### Table 1. Outline of the Guidelines Development Process

<table>
<thead>
<tr>
<th>Topic</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Goal of the guidelines</strong></td>
<td>Provide guidance to HIV care practitioners on the optimal use of antiretroviral agents (ARVs) for the treatment of HIV in adults and adolescents in the United States.</td>
</tr>
<tr>
<td><strong>Panel members</strong></td>
<td>The Panel is composed of approximately 45 voting members who have expertise in HIV care and research, and includes at least one representative from each of the following U.S. Department of Health and Human Services (HHS) agencies: Centers for Disease Control and Prevention (CDC), Food and Drug Administration (FDA), Health Resource Services Administration (HRSA), and National Institutes of Health (NIH). Approximately two-thirds of the Panel members are nongovernmental scientific members. The Panel also includes four to five community members with knowledge in HIV treatment and care. The U.S. government representatives are appointed by their respective agencies; other Panel members are selected after an open announcement to call for nominations. Each member serves on the Panel for a 4 year term with an option for reappointment for an additional term. See the <a href="#">Panel Roster</a> for a list of current Panel members.</td>
</tr>
<tr>
<td><strong>Financial disclosure</strong></td>
<td>All members of the Panel submit a written financial disclosure annually, reporting any association with manufacturers of ARV drugs or diagnostics used for management of HIV infections. A list of the latest disclosures is available on the AIDSinfo website (<a href="http://aidsinfo.nih.gov/contentfiles/AA_FinancialDisclosures.pdf">http://aidsinfo.nih.gov/contentfiles/AA_FinancialDisclosures.pdf</a>).</td>
</tr>
<tr>
<td><strong>Users of the guidelines</strong></td>
<td>HIV treatment providers</td>
</tr>
<tr>
<td><strong>Developer</strong></td>
<td>Panel on Antiretroviral Guidelines for Adults and Adolescents—a working group of the Office of AIDS Research Advisory Council (OARAC)</td>
</tr>
<tr>
<td><strong>Funding source</strong></td>
<td>Office of AIDS Research, NIH</td>
</tr>
<tr>
<td><strong>Evidence collection</strong></td>
<td>The recommendations in the guidelines are based on studies published in peer reviewed journals. On some occasions, particularly when new information may affect patient safety, unpublished data presented at major conferences or prepared by the FDA and/or manufacturers as warnings to the public may be used as evidence to revise the guidelines.</td>
</tr>
<tr>
<td><strong>Recommendation grading</strong></td>
<td>As described in <a href="#">Table 2</a></td>
</tr>
<tr>
<td><strong>Method of synthesizing data</strong></td>
<td>Each section of the guidelines is assigned to a working group of Panel members with expertise in the section’s area of interest. The working groups synthesize available data and propose recommendations to the Panel. The Panel discusses all proposals during monthly teleconferences. Recommendations endorsed by the Panel are included in the guidelines.</td>
</tr>
<tr>
<td><strong>Other guidelines</strong></td>
<td>These guidelines focus on antiretroviral therapy (ART) use for adults and adolescents with HIV. For more detailed discussion on the use of ART for children and prepubertal adolescents (SMR I – III), clinicians should refer to the Pediatric ARV Guidelines. These guidelines also include a brief discussion on the management of women of reproductive age and pregnant women.</td>
</tr>
<tr>
<td><strong>Update plan</strong></td>
<td>The Panel meets monthly by teleconference to review data that may warrant modification of the guidelines. Updates may be prompted by new drug approvals (or new indications, dosing formulations, or frequency of dosing), new safety or efficacy data, or other information that may have an impact on the clinical care of patients. In the event of new data of clinical importance, the Panel may post an interim announcement with recommendations on the AIDSinfo website until the guidelines can be updated with the appropriate changes. Updated guidelines are available on the AIDSinfo website (<a href="http://www.aidsinfo.nih.gov">http://www.aidsinfo.nih.gov</a>).</td>
</tr>
<tr>
<td><strong>Public comments</strong></td>
<td>A 2-week public comment period follows release of the updated guidelines on the AIDSinfo website. The Panel reviews comments received to determine whether additional revisions to the guidelines are indicated. The public may also submit comments to the Panel at any time at <a href="mailto:contactus@aidsinfo.nih.gov">contactus@aidsinfo.nih.gov</a>.</td>
</tr>
</tbody>
</table>
### Table 2. Rating Scheme for Recommendations

<table>
<thead>
<tr>
<th>Strength of Recommendation</th>
<th>Quality of Evidence for Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A:</strong> Strong recommendation for the statement</td>
<td>I: One or more randomized trials with clinical outcomes and/or validated laboratory endpoints</td>
</tr>
<tr>
<td><strong>B:</strong> Moderate recommendation for the statement</td>
<td>II: One or more well-designed, non-randomized trials or observational cohort studies with long-term clinical outcomes</td>
</tr>
<tr>
<td><strong>C:</strong> Optional recommendation for the statement</td>
<td>III: Expert opinion</td>
</tr>
<tr>
<td>Laboratory Test</td>
<td>Entry into Care</td>
</tr>
<tr>
<td>----------------</td>
<td>----------------</td>
</tr>
<tr>
<td>HIV Serology</td>
<td>√</td>
</tr>
<tr>
<td>CD4 Count</td>
<td>√</td>
</tr>
<tr>
<td>HIV Viral Load</td>
<td>√</td>
</tr>
<tr>
<td>Resistance Testing</td>
<td>√</td>
</tr>
<tr>
<td>HLA-B*5701 Testing</td>
<td>√</td>
</tr>
<tr>
<td>Tropism Testing</td>
<td>√</td>
</tr>
<tr>
<td>Hepatitis B Serology</td>
<td>√</td>
</tr>
</tbody>
</table>

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV

Downloaded from https://aidsinfo.nih.gov/guidelines on 8/8/2018
<table>
<thead>
<tr>
<th>Laboratory Test</th>
<th>Entry into Care</th>
<th>ART Initiationa or Modification</th>
<th>2 to 8 Weeks After ART Initiation or Modification</th>
<th>Every 3 to 6 Months</th>
<th>Every 6 Months</th>
<th>Every 12 Months</th>
<th>Treatment Failure</th>
<th>Clinically Indicated</th>
<th>If ART Initiation is Delayedc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis C Screening (HCV antibody or, if indicated, HCV RNA)</td>
<td>√</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Repeat HCV screening for at-risk patientsx</td>
</tr>
<tr>
<td>Basic Chemistryl,m</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Every 6–12 months</td>
</tr>
<tr>
<td>ALT, AST, T. billirubin</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Every 6–12 months</td>
</tr>
<tr>
<td>CBC with Differential</td>
<td>√</td>
<td>√</td>
<td>If on ZDV</td>
<td>If on ZDV or if CD4 testing is done</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Every 3–6 months</td>
</tr>
<tr>
<td>Fasting Lipid Profilen</td>
<td>√</td>
<td>√</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>If normal at baseline, annually</td>
</tr>
<tr>
<td>Fasting Glucose or Hemoglobin A1C</td>
<td>√</td>
<td>√</td>
<td>If abnormal at last measurement</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>If normal at baseline, annually</td>
</tr>
<tr>
<td>Uranalysism,o</td>
<td>√</td>
<td>√</td>
<td>If on TAF or TDF</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Pregnancy Test</td>
<td></td>
<td></td>
<td>In women of child-bearing potential</td>
<td></td>
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</tr>
</tbody>
</table>

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV

Downloaded from https://aidsinfo.nih.gov/guidelines on 8/8/2018
This table pertains to laboratory tests done to select an ARV regimen and monitor for treatment responses or ART toxicities. Please refer to the HIV Primary Care guidelines for guidance on other laboratory tests generally recommended for primary health care maintenance of HIV patients.

If ART initiation occurs soon after HIV diagnosis and entry into care, repeat baseline laboratory testing is not necessary.

ART is indicated for all individuals with HIV and should be started as soon as possible. However, if ART initiation is delayed, patients should be retained in care, with periodic monitoring as noted above.

If HIV RNA is detectable at 2 to 8 weeks, repeat every 4 to 8 weeks until viral load is suppressed to <200 copies/mL. Thereafter, repeat every 3 to 6 months.

In patients on ART, viral load typically is measured every 3 to 4 months. However, for adherent patients with consistently suppressed viral load and stable immunologic status for more than 2 years, monitoring can be extended to 6-month intervals.

Based on current rates of transmitted drug resistance to different ARV medications, standard genotypic drug-resistance testing in ARV-naive persons should focus on testing for mutations in the reverse transcriptase and protease genes. If transmitted INSTI resistance is a concern, providers should also test for resistance mutations to this class of drugs. In ART-naive patients who do not immediately begin ART, repeat testing before initiation of ART is optional if resistance testing was performed at entry into care. In virologically suppressed patients who are switching therapy because of toxicity or for convenience, viral amplification will not be possible; therefore, resistance testing should not be performed. Results from prior resistance testing can be helpful in constructing a new regimen.

If patient has HBV infection (as determined by a positive HBsAg or HBV DNA test), TDF or TAF plus either FTC or 3TC should be used as part of the ARV regimen to treat both HBV and HIV infections.

If HBsAg, HBsAb, and HbcAb are negative, hepatitis B vaccine series should be administered. Refer to HIV Primary Care and Opportunistic Infections guidelines for more detailed recommendations.

Most patients with isolated HbcAb have resolved HBV infection with loss of HBsAb. Consider performing an HBV viral load for confirmation. If the HBV viral load is positive, the patient may be acutely infected (and will usually display other signs of acute hepatitis) or chronically infected. If negative, the patient should be vaccinated. Refer to HIV Primary Care and the Adult and Adolescent Opportunistic Infections Guidelines for more detailed recommendations.

HCV antibody may not be adequate for screening in the setting of recent HCV infection (acquisition within past 6 months), or advanced immunodeficiency (CD4 count <100 cells/mm$^3$). HCV RNA screening is indicated in persons who have been successfully treated for HCV or who spontaneously cleared prior infection. HCV antibody-negative patients with elevated ALT may need HCV RNA testing.

Injection drug users, persons with a history of incarceration, men with HIV who have unprotected sex with men, and persons with percutaneous/parenteral exposure to blood in unregulated settings are at risk of HCV infection.

Serum Na, K, HCO$_3^-$, Cl, BUN, creatinine, glucose (preferably fasting), and creatinine-based estimated glomerular filtration rate. Serum phosphorus should be monitored in patients with chronic kidney disease who are on TAF- or TDF-containing regimens.

Consult the Guidelines for the Management of Chronic Kidney Disease in HIV-Infected Patients: Recommendations of the HIV Medicine Association of the Infectious Diseases Society of America for recommendations on managing patients with renal disease. More frequent monitoring may be indicated for patients with evidence of kidney disease (e.g., proteinuria, decreased glomerular dysfunction) or increased risk of renal insufficiency (e.g., patients with diabetes, hypertension).

Consult the National Lipid Association's recommendations for management of patients with dyslipidemia.

Urine glucose and protein should be assessed before initiating TAF- or TDF-containing regimens, and monitored during treatment with these regimens.

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; ALT = alanine aminotransferase; ART = antiretroviral therapy; AST = aspartate aminotransferase; BUN = blood urea nitrogen; CBC = complete blood count; CD4 = CD4 T lymphocyte; Cl = chloride; FTC = emtricitabine; HbcAb = hepatitis B core antibody; HBsAb = hepatitis B surface antibody; HBsAg = hepatitis B surface antigen; HBV = hepatitis B virus; HCO$_3^-$ = bicarbonate; HCV = hepatitis C virus; INSTI = integrase strand transfer inhibitor; K = potassium; Na = sodium; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; ZDV = zidovudine
Table 4. Recommendations on the Indications and Frequency of Viral Load and CD4 Count Monitoring<sup>a</sup>

<table>
<thead>
<tr>
<th>Clinical Scenario</th>
<th>Viral Load Monitoring</th>
<th>CD4 Count Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before initiating ART</td>
<td>At entry into care (&lt;sup&gt;AIII&lt;/sup&gt;)</td>
<td>At entry into care (&lt;sup&gt;AI&lt;/sup&gt;)</td>
</tr>
<tr>
<td></td>
<td>If ART initiation is deferred, repeat before initiating ART (&lt;sup&gt;AIII&lt;/sup&gt;)</td>
<td>If ART is deferred, every 3 to 6 months&lt;sup&gt;b&lt;/sup&gt; (&lt;sup&gt;AIII&lt;/sup&gt;)</td>
</tr>
<tr>
<td></td>
<td>In patients not initiating ART, repeat testing is optional (&lt;sup&gt;CIII&lt;/sup&gt;)</td>
<td>(AIII)</td>
</tr>
<tr>
<td>After initiating ART</td>
<td>Preferably within 2 to 4 weeks (and no later than 8 weeks) after initiation of ART (&lt;sup&gt;AIII&lt;/sup&gt;); thereafter, every 4 to 8 weeks until viral load is suppressed (&lt;sup&gt;BII&lt;/sup&gt;).</td>
<td>3 months after initiation of ART (&lt;sup&gt;AIII&lt;/sup&gt;)</td>
</tr>
<tr>
<td>After modifying ART because of drug toxicities or for regimen simplification in a patient with viral suppression</td>
<td>4 to 8 weeks after modification of ART to confirm effectiveness of new regimen (&lt;sup&gt;AIII&lt;/sup&gt;)</td>
<td>Monitor according to prior CD4 count and duration on ART, as outlined below.</td>
</tr>
<tr>
<td>After modifying ART because of virologic failure</td>
<td>Preferably within 2 to 4 weeks (and no later than 8 weeks) after modification (&lt;sup&gt;AII&lt;/sup&gt;); thereafter, every 4 to 8 weeks until viral load is suppressed (&lt;sup&gt;BII&lt;/sup&gt;). If viral suppression is not possible, repeat viral load every 3 months or more frequently if indicated (&lt;sup&gt;AIII&lt;/sup&gt;).</td>
<td>Every 3 to 6 months (&lt;sup&gt;AI&lt;/sup&gt;)</td>
</tr>
<tr>
<td>During the first 2 years of ART</td>
<td>Every 3 to 4 months (&lt;sup&gt;AIII&lt;/sup&gt;)</td>
<td>Every 3 to 6 months&lt;sup&gt;c&lt;/sup&gt; (&lt;sup&gt;BII&lt;/sup&gt;)</td>
</tr>
<tr>
<td>After 2 years of ART (VL consistently suppressed, CD4 consistently 300-500 cells/mm&lt;sup&gt;3&lt;/sup&gt;)</td>
<td>Can extend to every 6 months for patients with consistent viral suppression for ≥2 years (&lt;sup&gt;AII&lt;/sup&gt;).</td>
<td>Every 12 months (&lt;sup&gt;BII&lt;/sup&gt;)</td>
</tr>
<tr>
<td>After 2 years of ART (VL consistently suppressed, CD4 consistently &gt;500 cells/mm&lt;sup&gt;3&lt;/sup&gt;)</td>
<td></td>
<td>Optional (&lt;sup&gt;CIII&lt;/sup&gt;)</td>
</tr>
<tr>
<td>While on ART with detectable viremia (VL repeatedly &gt;200 copies/mL)</td>
<td>Every 3 months (&lt;sup&gt;AIII&lt;/sup&gt;) or more frequently if clinically indicated (see Virologic Failure).</td>
<td>Every 3 to 6 months (&lt;sup&gt;AIII&lt;/sup&gt;)</td>
</tr>
<tr>
<td>Change in clinical status (e.g., new HIV clinical symptom or initiation of interferon, chronic systemic corticosteroids, or antineoplastic therapy)</td>
<td>Every 3 months (&lt;sup&gt;AIII&lt;/sup&gt;)</td>
<td>Perform CD4 count and repeat as clinically indicated&lt;sup&gt;c&lt;/sup&gt; (&lt;sup&gt;AIII&lt;/sup&gt;)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Monitoring of lymphocyte subsets other than CD4 (e.g., CD8, CD19) has not proven clinically useful, adds to costs, and is not routinely recommended (<sup>BIII</sup>).

<sup>b</sup> Some experts may repeat CD4 count every 3 months in patients with low baseline CD4 count (<200–300 cells/mm<sup>3</sup>) before ART but every 6 months in those who initiated ART at higher CD4 cell count (e.g., >300 cells/mm<sup>3</sup>).

<sup>c</sup> The following are examples of clinically indicated scenarios: changes in a patient’s clinical status that may decrease CD4 count and thus prompt initiation of prophylaxis for opportunistic infections (OI), such as new HIV-associated symptoms, or initiation of treatment with medications which are known to reduce CD4 cell count.
Table 5. Recommendations for Using Drug-Resistance Assays (page 1 of 2)

<table>
<thead>
<tr>
<th>Clinical Setting and Recommendation</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>In acute or recent (early) HIV infection:</strong> Drug-resistance testing is recommended (AII). A genotypic assay is generally preferred (AII). Treatment should not be delayed while awaiting results of resistance testing (AII). If ART is deferred, repeat resistance testing may be considered when therapy is initiated (CIII). A genotypic assay is generally preferred (AIII).</td>
<td>Drug-resistance testing can determine whether drug-resistant virus was transmitted. The initial regimen can be modified once resistance test results are available. Genotypic testing is preferred to phenotypic testing because of lower cost, faster turnaround time, and greater sensitivity for detecting mixtures of wild-type and resistant virus. Repeat testing when ART is initiated may be considered because the patient may have acquired a drug-resistant virus (i.e., superinfection).</td>
</tr>
<tr>
<td><strong>In ART-naive patients with chronic HIV infection:</strong> Drug-resistance testing is recommended at entry into HIV care to guide selection of initial ART (AII). A genotypic assay is generally preferred (AII). If an INSTI is considered for an ART-naive patient and transmitted INSTI resistance is a concern, providers should supplement standard resistance testing with a specific INSTI genotypic resistance assay (BIII). If therapy is deferred, repeat resistance testing may be considered before initiation of ART (CIII). A genotypic assay is generally preferred (AIII). If use of a CCR5 antagonist is being considered, a co-receptor tropism assay should be performed (AII) (see Co-receptor Tropism Assays).</td>
<td>Transmitted HIV with baseline resistance to at least 1 drug is seen in 10% to 17% of patients, and suboptimal virologic responses may be seen in patients with baseline resistant mutations. Some drug-resistance mutations can remain detectable for years in untreated patients with chronic HIV infection. Genotypic assays provide information on resistance to NRTIs, NNRTIs, PIs, and INSTIs. In some circumstances, INSTI-resistance tests need to be ordered separately (clinicians should check with the testing laboratory). Currently, transmitted INSTI resistance is infrequent, but the risk of a patient acquiring INSTI-resistant strains may be greater in certain known exposure settings. Repeat testing before initiation of ART may be considered because the patient may have acquired a drug-resistant virus (i.e., a superinfection). Genotypic testing is preferred to phenotypic testing because of lower cost, faster turnaround time, and greater sensitivity for detecting mixtures of wild-type and resistant virus.</td>
</tr>
<tr>
<td><strong>In patients with virologic failure:</strong> Drug-resistance testing is recommended in patients on combination ART with HIV RNA levels &gt;1,000 copies/mL (AII). In patients with HIV RNA levels &gt;500 copies/mL but &lt;1,000 copies/mL, testing may not be successful but should still be considered (BII). A standard genotypic resistance assay is generally preferred for patients experiencing virologic failure on their first or second regimens (AII). When virologic failure occurs while a patient is on an INSTI-based regimen, genotypic testing for INSTI resistance should be performed to determine whether to include drugs from this class in subsequent regimens (AII). If use of a CCR5 antagonist is being considered, a co-receptor tropism assay should be performed (AII) (see Co-receptor Tropism Assays). Adding phenotypic testing to genotypic testing is generally preferred in patients with known or suspected complex drug-resistance patterns, particularly to PIs (BIII).</td>
<td>Drug-resistance testing can help determine the role of resistance in drug failure and maximize the clinician’s ability to select active drugs for the new regimen. Drug-resistance testing should be performed while the patient is taking prescribed ARV drugs or, if not possible, within 4 weeks after discontinuing therapy (AII). Genotypic testing is preferred to phenotypic testing because of lower cost, faster turnaround time, and greater sensitivity for detecting mixtures of wild-type and resistant HIV. Genotypic assays provide information on resistance to NRTI-, NNRTI-, PI-, and INSTI-associated mutations. In some circumstances, INSTI resistance tests need to be ordered separately (clinicians should check with the testing laboratory). Phenotypic testing can provide additional useful information in patients with complex drug resistance mutation patterns, particularly to PIs.</td>
</tr>
<tr>
<td><strong>In patients with suboptimal suppression of viral load:</strong> Drug-resistance testing is recommended in patients with suboptimal viral load suppression after initiation of ART (AII).</td>
<td>Testing can determine the role of resistance and thus help the clinician identify the number of active drugs available for a new regimen.</td>
</tr>
<tr>
<td>Clinical Setting and Recommendation</td>
<td>Rationale</td>
</tr>
<tr>
<td>------------------------------------</td>
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</tr>
<tr>
<td><strong>Drug-Resistance Assay Recommended</strong></td>
<td></td>
</tr>
<tr>
<td>In pregnant women with HIV: Genotypic resistance testing is recommended for all pregnant women before initiation of ART (AIII) and for those entering pregnancy with detectable HIV RNA levels while on therapy (AI).</td>
<td>The goal of ART in pregnant women with HIV is to achieve maximal viral suppression for treatment of maternal HIV infection and for prevention of perinatal transmission of HIV. Genotypic resistance testing will assist the clinician in selecting the optimal regimen for the patient. However, treatment should not be delayed while awaiting results of resistance testing. The initial regimen can be modified once resistance test results are available.</td>
</tr>
<tr>
<td><strong>Drug-Resistance Assay Not Usually Recommended</strong></td>
<td></td>
</tr>
<tr>
<td>After therapy is discontinued: Drug-resistance testing is not usually recommended more than 4 weeks after ARV drugs are discontinued (BIII).</td>
<td>Drug-resistance mutations may become minor species in the absence of selective drug pressure, and available assays may not detect minor drug-resistant species. If testing is performed in this setting, the detection of drug resistance may be of value; however, the absence of resistance does not rule out the presence of minor drug-resistant species.</td>
</tr>
<tr>
<td>In patients with low HIV RNA levels: Drug-resistance testing is not usually recommended in patients with a plasma viral load &lt;500 copies/mL (AIII).</td>
<td>Resistance assays cannot be consistently performed given low HIV RNA levels.</td>
</tr>
</tbody>
</table>

**Key to Acronyms:** ART = antiretroviral therapy; ARV = antiretroviral; INSTI = integrase strand transfer inhibitors; NNRTI = non-nucleoside reverse-transcriptase inhibitors; NRTI = nucleoside reverse-transcriptase inhibitors; PI = protease inhibitor
Table 6. Recommended Antiretroviral Regimens for Initial Therapy

Selection of a regimen should be individualized based on virologic efficacy, potential adverse effects, pill burden, dosing frequency, drug-drug interaction potential, comorbid conditions, cost, access, and resistance test results. Drug classes and regimens within each class are arranged first by evidence rating, and, when ratings are equal, in alphabetical order. Table 7 provides ARV recommendations based on specific clinical scenarios.

Recommended Initial Regimens for Most People with HIV

Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use.

<table>
<thead>
<tr>
<th>INSTI + 2 NRTIs:</th>
</tr>
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<tbody>
<tr>
<td>• DTG/ABC/3TC (AI) — if HLA-B*5701 negative</td>
</tr>
<tr>
<td>• DTG + tenofovir/FTC (AI for both TAF/FTC and TDF/FTC)</td>
</tr>
<tr>
<td>• EVG/c/tenofovir/FTC (AI for both TAF/FTC and TDF/FTC)</td>
</tr>
<tr>
<td>• RAL + tenofovir/FTC (AI for TDF/FTC, All for TAF/FTC)</td>
</tr>
</tbody>
</table>

Recommended Initial Regimens in Certain Clinical Situations

These regimens are effective and tolerable, but have some disadvantages when compared with the regimens listed above, or have less supporting data from randomized clinical trials. However, in certain clinical situations, one of these regimens may be preferred (see Table 7 for examples).

Boosted PI + 2 NRTIs: (In general, boosted DRV is preferred over boosted ATV)

- (DRV/c or DRV/r) + tenofovir/FTC (AI for DRV/r and All for DRV/c)
- (ATV/c or ATV/r) + tenofovir/FTC (BI)
- (DRV/c or DRV/r) + ABC/3TC — if HLA-B*5701-negative (BII)
- (ATV/c or ATV/r) + ABC/3TC — if HLA-B*5701-negative and HIV RNA <100,000 copies/mL (CI for ATV/r and CIII for ATV/c)

NNRTI + 2 NRTIs:

- EFV + tenofovir/FTC (BI for EFV/TDF/FTC and BII for EFV + TAF/FTC)
- RPV/tenofovir/FTC (BI)

INSTI + 2 NRTIs:

- • RAL + ABC/3TC (CII) — if HLA-B*5701-negative and HIV RNA < 100,000 copies/mL

Regimens to Consider when ABC, TAF, and TDF Cannot be Used:

- DRV/r + RAL (BID) (CI) — if HIV RNA <100,000 copies/mL and CD4 >200 cells/mm³
- • LPV/r + 3TC (BID)² (CI)

* 3TC may be substituted for FTC, or vice versa, if a non–fixed-dose NRTI combination is desired.

¹ TAF and TDF are two forms of tenofovir approved by the FDA. TAF has fewer bone and kidney toxicities than TDF, while TDF is associated with lower lipid levels. Safety, cost, and access are among the factors to consider when choosing between these drugs.

² RAL can be given as 400 mg BID or 1200 mg (two 600-mg tablets) once daily.

³ Several other NRTI-limiting treatment strategies are under investigation. See the section titled Selected Strategies That Are Under Evaluation and Not Yet Recommended below for discussion regarding these regimens.

⁴ LPV/r plus 3TC is the only boosted PI plus 3TC regimen with published 48-week data in a randomized controlled trial in ART-naive patients. Limitations of LPV/r plus 3TC include twice-daily dosing, high pill burden, and greater rates of gastrointestinal side effects than other PIs.

Note: The following are available as coformulated drugs: ABC/3TC, ATV/c, DRV/c, DTG/ABC/3TC, EFV/TDF/FTC, EVG/c/TAF/FTC, EVG/c/TDF/FTC, LPV/r, RPV/TAF/FTC, RPV/TDF/FTC, TAF/FTC, and TDF/FTC.

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BID = twice daily; CD4 = CD4 T lymphocyte; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FDA = Food and Drug Administration; FTC = emtricitabine; HLA = human leukocyte antigen; INSTI = integrase strand transfer inhibitor; LPV/r = lopinavir/ritonavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; RAL = raltegravir; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV

Downloaded from https://aidsinfo.nih.gov/guidelines on 8/8/2018
This table is designed to guide clinicians in choosing an initial ARV regimen according to various patient and regimen characteristics and specific clinical scenarios. When more than one scenario applies to a person with HIV, clinicians should review considerations for each relevant scenario and use their clinical judgment to select the most appropriate regimen. This table is intended to guide the initial choice of regimen. However, if a person is doing well on a particular regimen, it is not necessary to switch to another regimen based on the scenarios outlined in this table. Please see Table 8 for additional information regarding the advantages and disadvantages of particular ARV medications.

<table>
<thead>
<tr>
<th>Pre-ART Characteristics</th>
<th>Clinical Scenario</th>
<th>Consideration(s)</th>
<th>Rationale/Comments</th>
</tr>
</thead>
</table>
| CD4 count <200 cells/mm³ | Do Not Use the Following Regimens:  
  • RPV-based regimens  
  • DRV/r + RAL | A higher rate of virologic failure has been observed in those with low pretreatment CD4 count. |
| HIV RNA >100,000 copies/mL | Do Not Use the Following Regimens:  
  • RPV-based regimens  
  • ABC/3TC with EFV or ATV/r  
  • DRV/r + RAL | Higher rates of virologic failure have been observed in those with high pretreatment HIV RNA. |
| HLA-B*5701-positive | Do not use ABC-containing regimens. | Abacavir hypersensitivity, a potentially fatal reaction, is highly associated with positivity for the HLA-B*5701 allele. |

**ARV must be started before HIV drug resistance results are available (e.g., in a person with acute HIV or when a rapid initiation of ART is warranted). See Initiation of Antiretroviral Therapy.**

<table>
<thead>
<tr>
<th>ART-Specific Characteristics</th>
<th>Clinical Scenario</th>
<th>Consideration(s)</th>
<th>Rationale/Comments</th>
</tr>
</thead>
</table>
| A one-pill, once-daily regimen is desired. | STR Options Include:  
  • DTG/ABC/3TC  
  • EFV/TDF/FTC  
  • EVG/c/TAF/FTC  
  • EVG/c/TDF/FTC  
  • RPV/TAF/FTC  
  • RPV/TDF/FTC | Do not use RPV-based regimens if HIV RNA >100,000 copies/mL and CD4 count <200/mm³. | Since RPV-containing STRs are smaller in size than other STRs, they may be considered when a person has difficulty swallowing a larger pill. |
| | | Do not use DTG/ABC/3TC if patient is HLA-B*5701-positive. | |
| | Regimens that Can be Taken Without Regard to Food:  
  • RAL- or DTG-based regimens | Oral bioavailability of these regimens is not significantly affected by food. |
### Table 7. Antiretroviral Regimen Considerations as Initial Therapy based on Specific Clinical Scenarios

<table>
<thead>
<tr>
<th>Patient or Regimen Characteristics</th>
<th>Clinical Scenario</th>
<th>Consideration(s) Rationale/Comments</th>
</tr>
</thead>
</table>
| **ART-Specific Characteristics, continued** | Food effects, continued | Regimens that Should be Taken with Food:  
- ATV/r- or ATV/c-based regimens  
- DRV/r- or DRV/c-based regimens  
- EVG/c/TAF/FTC  
- EVG/c/TDF/FTC  
- RPV-based regimens  
Rationale: Food improves absorption of these regimens. RPV-containing regimens should be taken with at least 390 calories of food. |
| | |  
Regimens that Should be Taken on an Empty Stomach:  
- EFV-based regimens  
Rationale: Food increases EFV absorption and may increase CNS side effects. |
| **Presence of Other Conditions** | Chronic kidney disease (defined as CrCl <60 mL/min) | Avoid TDF. Use ABC or TAF.  
ABC may be used if HLA-B*5701–negative. If HIV RNA >100,000 copies/mL, do not use ABC/3TC + (EFV or ATV/r).  
TAF may be used if CrCl >30 mL/min.  
Consider avoiding ATV.  
Other Options When ABC or TAF Cannot be Used:  
- LPV/r + 3TC; or  
- RAL + DRV/r (if CD4 count >200 cells/mm³, HIV RNA <100,000 copies/mL)  
- See text for discussion of alternative NRTI-limiting regimens. |
| | Liver disease with cirrhosis | Some ARVs are contraindicated or may require dosage modification in patients with Child-Pugh class B or C disease.  
Refer to Appendix B, Table 7 for specific dosing recommendations.  
Patients with cirrhosis should be carefully evaluated by an expert in advanced liver disease. |
| | Osteoporosis | Avoid TDF.  
Use ABC or TAF.  
ABC may be used if HLA-B*5701–negative. If HIV RNA >100,000 copies/mL, do not use ABC/3TC + (EFV or ATV/r).  
TDF is associated with decreases in bone mineral density along with renal tubulopathy, urine phosphate wasting, and resultant osteomalacia. TAF and ABC are associated with smaller declines in bone mineral density than TDF. |
| | Psychiatric illnesses | Consider avoiding EFV- and RPV-based regimens.  
Patients on INSTI-based regimens with pre-existing psychiatric conditions should be closely monitored.  
EFV and RPV can exacerbate psychiatric symptoms and may be associated with suicidality.  
INSTIs have been associated with adverse neuropsychiatric effects in some retrospective cohort studies and case series. |
### Table 7. Antiretroviral Regimen Considerations as Initial Therapy based on Specific Clinical Scenarios (page 3 of 4)

<table>
<thead>
<tr>
<th>Patient or Regimen Characteristics</th>
<th>Clinical Scenario</th>
<th>Consideration(s)</th>
<th>Rationale/Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence of Other Conditions, continued</td>
<td>HIV-associated dementia (HAD)</td>
<td>Avoid EFV-based regimens if possible.</td>
<td>EFV-related neuropsychiatric effects may confound assessment of ART's beneficial effects on improvement of HAD-related symptoms.</td>
</tr>
<tr>
<td></td>
<td>Narcotic replacement therapy required</td>
<td>If patient is receiving methadone, consider avoiding EFV-based regimens.</td>
<td>EFV reduces methadone concentrations and may lead to withdrawal symptoms.</td>
</tr>
<tr>
<td></td>
<td>High cardiac risk</td>
<td>DTG-, RAL- or RPV-based regimens may be advantageous in this setting.</td>
<td>An increased CV risk has been observed in some studies.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>If a boosted PI is the desired option, an ATV-based regimen may have advantages over a DRV-based regimen.</td>
<td>Observational cohort studies reported an association between some PIs (DRV, IDV, FPV, and LPV/r) and an increased risk of CV events, while this has not been seen with ATV (see text); further study is needed.</td>
</tr>
<tr>
<td></td>
<td>Cardiac QTc interval prolongation</td>
<td>Consider avoiding EFV- or RPV-based regimens if taking other medications with known risk of torsades de pointes, or in patients at higher risk of torsades de pointes.</td>
<td>High EFV or RPV concentrations may cause QT prolongation.</td>
</tr>
<tr>
<td></td>
<td>Hyperlipidemia</td>
<td>The Following ARV Drugs Have Been Associated with Dyslipidemia:</td>
<td>DTG, RAL, and RPV have fewer lipid effects.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• PI/r or PI/c</td>
<td>TDF has been associated with lower lipid levels than ABC or TAF.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• EFV</td>
<td>These regimens have a high genetic barrier to resistance.</td>
</tr>
<tr>
<td></td>
<td>Patients with history of poor adherence to ARV or inconsistent engagement in care</td>
<td>Consider boosted PI- or DTG-based regimens.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pregnancy</td>
<td>Refer to the Perinatal Guidelines for specific regimen recommendations.</td>
<td></td>
</tr>
<tr>
<td>Presence of Coinfections</td>
<td>HBV infection</td>
<td>Use TDF or TAF, with FTC or 3TC, whenever possible.</td>
<td>TDF, TAF, FTC, and 3TC are active against both HIV and HBV. 3TC- or FTC-associated HBV mutations can emerge rapidly when these drugs are used without another drug active against HBV.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TDF, TAF, FTC, and 3TC are active against both HIV and HBV. 3TC- or FTC-associated HBV mutations can emerge rapidly when these drugs are used without another drug active against HBV.</td>
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**Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV**
<table>
<thead>
<tr>
<th>Patient or Regimen Characteristics</th>
<th>Clinical Scenario</th>
<th>Consideration(s)</th>
<th>Rationale/Comments</th>
</tr>
</thead>
</table>
| Presence of Coinfections, continued | Treating TB disease with rifamycins                                                | TAF is **not recommended** with any rifamycin-containing regimen. | • Rifamycins may significantly reduce TAF exposure.  
  • Rifampin is a strong inducer of CYP3A4 and UGT1A1 enzymes, causing significant decrease in concentrations of PIs, INSTIs, and RPV.  
  • Rifampin has a less significant effect on EFV concentration than on other NNRTIs, PIs, and INSTIs.  
  • Rifabutin is a less potent inducer and is an option for patients receiving non-EFV-based regimens.  
  Refer to Tables 18a, b, d and e for dosing recommendations for rifamycins used with different ARV agents. |

*TAF and TDF are two approved forms of tenofovir. TAF has less bone and kidney toxicities than TDF, whereas TDF is associated with lower lipid levels. Safety, cost, and access are among the factors to consider when choosing between these drugs.*

**Key to Acronyms:** 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; BID = twice daily; c = cobicistat; CD4 = CD4 T lymphocyte; CNS = central nervous system; CrCl = creatinine clearance; CV = cardiovascular; CYP = cytochrome P; DRV = darunavir; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; FPV = fosamprenavir; FTC = emtricitabine; HBV = hepatitis B virus; HCV = hepatitis C virus; HLA = human leukocyte antigen; IDV = indinavir; INSTI = integrase strand transfer inhibitor; LPV = lopinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PI/r = ritonavir-boosted protease inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV or r = ritonavir; STR = single-tablet regimen; TAF = tenofovir alafenamide; TB = tuberculosis; TDF = tenofovir disoproxil fumarate; UGT = uridine diphosphate glucuronosyltransferase
Table 8. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy (page 1 of 4)

**Note:** All drugs within an ARV class are listed in alphabetical order.

<table>
<thead>
<tr>
<th>ARV Class</th>
<th>ARV Agent(s)</th>
<th>Advantage(s)</th>
<th>Disadvantage(s)</th>
</tr>
</thead>
</table>
| Dual-NRTI | ABC/3TC      | • Coformulated with DTG | • May cause life-threatening HSRs in patients positive for the HLA-B*5701 allele. As a result, HLA-B*5701 testing is required before use.  
• In the ACTG 5202 study, patients with baseline HIV RNA ≥100,000 copies/mL showed inferior virologic responses when ABC/3TC was given with EFV or ATV/r as opposed to TDF/FTC. This difference was not seen when ABC/3TC was used in combination with DTG.  
• ABC use has been associated with CV disease and cardiac events in some, but not all, observational studies. |
|           | TAF/FTC      | • Coformulated with EVG/c or RPV  
• Active against HBV; a recommended dual-NRTI option for patients with HIV/HBV coinfection  
• Smaller decline in renal function, less proteinuria, and smaller reductions in BMD than after initiation of TDF/FTC  
• Approved for patients with eGFR ≥30 mL/min | • TDF is associated with lower lipid levels than TAF, perhaps because TDF results in higher plasma levels of tenofovir, which lowers lipids. |
|           | TDF/FTC      | • Coformulated with EFV, EVG/c, and RPV as STRs  
• Active against HBV; a recommended dual-NRTI option for patients with HIV/HBV coinfection  
• Better virologic responses than with ABC/3TC in patients with baseline viral load ≥100,000 copies/mL when combined with ATV/r or EFV  
• Associated with lower lipid levels than ABC or TAF | • Renal toxicity, including proximal tubulopathy and acute or chronic renal insufficiency  
• Osteomalacia has been reported as a consequence of proximal tubulopathy.  
• Decreases BMD more than other NRTI combinations |
| INSTI     | DTG          | • Higher barrier to resistance than EVG or RAL  
• Coformulated with ABC and 3TC  
• No food requirement  
• No CYP3A4 interactions  
• Favorable lipid profile | • Oral absorption of DTG can be reduced by simultaneous administration with drugs containing polyvalent cations (e.g., Al, Ca, or Mg-containing antacids or supplements, or multivitamin tablets with minerals). See dosing recommendations in Table 18d.  
• Inhibits renal tubular secretion of Cr and can increase serum Cr without affecting glomerular function  
• UGT substrate; potential for drug interactions (see Table 18d)  
• Depression and suicidal ideation (rare; usually in patients with pre-existing psychiatric conditions) |
<table>
<thead>
<tr>
<th>ARV Class</th>
<th>ARV Agent(s)</th>
<th>Advantage(s)</th>
<th>Disadvantage(s)</th>
</tr>
</thead>
</table>
| INSTI, continued | EVG/c | • Coformulated with TDF/FTC or TAF/FTC  
• Compared with ATV/r, causes smaller increases in total and LDL cholesterol | • EVG/c/TDF/FTC is only recommended for patients with baseline CrCl ≥ 70 mL/min; this regimen should be discontinued if CrCl decreases to <50 mL/min.  
• COBI is a potent CYP3A4 inhibitor, which can result in significant interactions with CYP3A substrates.  
• Oral absorption of EVG can be reduced by simultaneous administration with drugs containing polyvalent cations (e.g., Al, Ca, or Mg-containing antacids or supplements, or multivitamin tablets with minerals). See dosing recommendations in Table 18d.  
• COBI inhibits active tubular secretion of Cr and can increase serum Cr, without affecting renal glomerular function.  
• Lower genetic barrier to resistance than boosted PI- or DTG-based regimens  
• Food requirement  
• Depression and suicidal ideation (rare; usually in patients with pre-existing psychiatric conditions) | |
| | RAL | • Compared to other INSTIs, has longest post-marketing experience  
• No food requirement  
• No CYP3A4 interactions  
• Favorable lipid profile | • Lower genetic barrier to resistance than boosted PI- or DTG-based regimens  
• Increases in creatine kinase, myopathy, and rhabdomyolysis have been reported.  
• Rare cases of severe HSRs (including SJS and TEN) have been reported.  
• Higher pill burden than other INSTI-based regimens  
• No fixed-dose combination formulation  
• Oral absorption of RAL can be reduced by simultaneous administration with drugs containing polyvalent cations (e.g., Al, Ca, or Mg-containing antacids or supplements, or multivitamin tablets with minerals). See dosing recommendations in Table 18d.  
• UGT substrate; potential for drug interactions (see Table 18d)  
• Depression and suicidal ideation (rare; usually in patients with pre-existing psychiatric conditions) |
### Table 8. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy (page 3 of 4)

<table>
<thead>
<tr>
<th>ARV Class</th>
<th>ARV Agent(s)</th>
<th>Advantage(s)</th>
<th>Disadvantage(s)</th>
</tr>
</thead>
</table>
| NNRTIs    | EFV          | • Coformulated with TDF/FTC  
• Long-term clinical experience  
• EFV-based regimens (except for EFV + ABC/3TC) have well-documented efficacy in patients with high HIV RNA. | • Short-and long-term neuropsychiatric (CNS) side effects, including depression and, in some studies, suicidality  
• Teratogenic in nonhuman primates  
• Dyslipidemia  
• Rash  
• QTc interval prolongation; consider an alternative to EFV in patients taking medications with known risk of causing TdP, or in those at higher risk of TdP.  
• Transmitted resistance more common than with PIs and INSTIs  
• Greater risk of resistance at the time of treatment failure than with PIs  
• Potential for CYP450 drug interactions (see Tables 18b and 19a)  
• Should be taken on an empty stomach (food increases drug absorption and CNS toxicities) |
|           | RPV          | • Coformulated with TDF/FTC and TAF/FTC  
• RPV/TDF/FTC and RPV/TAF/FTC have smaller pill size than other coformulated ARV drugs  
• Compared with EFV:  
• Fewer CNS adverse effects  
• Fewer lipid effects  
• Fewer rashes | • Not recommended in patients with pre-ART HIV RNA >100,000 copies/mL or CD4 count <200 cells/mm³ because of higher rate of virologic failure in these patients  
• Depression and suicidality  
• QTc interval prolongation; consider an alternative to RPV in patients taking medications with known risk of causing TdP, or in those at higher risk of TdP.  
• Rash  
• Transmitted resistance more common than with PIs and INSTIs  
• More NNRTI-, TDF-, and 3TC-associated mutations at virologic failure than with regimen containing EFV and 2 NRTIs  
• Potential for CYP450 drug interactions (see Tables 18b and 19a)  
• Meal requirement (>390 kcal)  
• Requires acid for adequate absorption  
• Contraindicated with PPIs  
• Use with H2 antagonists or antacids with caution (see Table 18a for detailed dosing information). |
| PIs       | ATV/c or ATV/r | • Higher genetic barrier to resistance than NNRTIs, EGV, and RAL  
• PI resistance at the time of treatment failure uncommon with PK-enhanced PIs  
• ATV/c and ATV/r have similar virologic activity and toxicity profiles  
• Observational cohort studies have found an association between some PIs (DRV, LPV/r, FPV, IDV) and an increased risk of CV events, while this has not been seen with ATV. Further study is needed. See text for discussion. | • Commonly causes indirect hyperbilirubinemia, which may manifest as scleral icterus or jaundice  
• Food requirement  
• Absorption depends on food and low gastric pH (see Table 18a for interactions with H2 antagonists, antacids, and PPIs)  
• Nephrolithiasis, cholelithiasis, nephrotoxicity  
• GI adverse effects  
• CYP3A4 inhibitors and substrates: potential for drug interactions (see Table 18a) |
<table>
<thead>
<tr>
<th>ARV Class</th>
<th>ARV Agent(s)</th>
<th>Advantage(s)</th>
<th>Disadvantage(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PIs, continued</strong></td>
<td><strong>ATV/c</strong> (Specific considerations)</td>
<td>• Coformulated tablet</td>
<td>• COBI inhibits active tubular secretion of Cr and can increase serum Cr, without affecting renal glomerular function. • Coadministration with TDF is not recommended in patients with CrCl &lt;70 mL/min • Less long-term clinical experience than for ATV/r • COBI (like RTV) is a potent CYP3A4 inhibitor, which can result in significant interactions with CYP3A substrates.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Higher genetic barrier to resistance than NNRTIs, EVG, and RAL • PI resistance at the time of treatment failure uncommon with PK-enhanced PIs</td>
<td>• Skin rash • Food requirement • GI adverse effects • CYP3A4 inhibitors and substrates: potential for drug interactions (see Table18a) • Increased CV risk in one observational cohort study</td>
</tr>
<tr>
<td><strong>DRV/c or DRV/r</strong></td>
<td><strong>DRV/c</strong> (Specific considerations)</td>
<td>• Coformulated tablet</td>
<td>• COBI inhibits active tubular secretion of Cr and can increase serum Cr, without affecting renal glomerular function. • Coadministration with TDF is not recommended in patients with CrCl &lt;70 mL/min • Approval primarily based on PK data comparable to that for DRV/r rather than on trials comparing the efficacy of DRV/c and DRV/r • COBI (like RTV) is a potent CYP3A4 inhibitor, which can result in significant interactions with CYP3A substrates.</td>
</tr>
<tr>
<td></td>
<td><strong>LPV/r</strong></td>
<td>• Only RTV-coformulated PI • No food requirement</td>
<td>• Requires 200 mg per day of RTV • Possible higher risk of MI associated with cumulative use of LPV/r • PR and QT interval prolongation have been reported. Use with caution in patients at risk of cardiac conduction abnormalities or in patients receiving other drugs with similar effect. • Possible nephrotoxicity • CYP3A4 inhibitors and substrates: potential for drug interactions (see Table18a)</td>
</tr>
</tbody>
</table>

**Key to Acronyms:** 3TC = lamivudine; ABC = abacavir; Al = aluminum; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; BMD = bone mineral density; Ca = calcium; CD4 = CD4 T lymphocyte; CNS = central nervous system; COBI or c = cobicistat; Cr = creatinine; CrCl = creatinine clearance; CV = cardiovascular; CYP = cytochrome P; DRV = darunavir; DTG = dolutegravir; eGFR = estimated glomerular filtration rate; EFV = efavirenz; EVG = elvitegravir; FPV = fosamprenavir; FTC = emtricitabine; GI = gastrointestinal; HBV = hepatitis B virus; HLA = human leukocyte antigen; HSR = hypersensitivity reaction; IDV = indinavir; INSTI = integrase strand transfer inhibitor; LDL = low-density lipoprotein; LPV = lopinavir; Mg = magnesium; MI = myocardial infarction; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PK = pharmacokinetic; PPI = proton pump inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV or r = ritonavir; SJS = Stevens-Johnson syndrome; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TdP = torsades de pointes; TEN = toxic epidermal necrosis; UGT = uridine diphosphate glucuronosyltransferase
### Table 9. Antiretroviral Components or Regimens Not Recommended as Initial Therapy

<table>
<thead>
<tr>
<th>ARV Components or Regimens</th>
<th>Reasons for Not Recommending as Initial Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NRTIs</strong></td>
<td></td>
</tr>
<tr>
<td>ABC/3TC/ZDV (Coformulated) As triple-NRTI combination regimen</td>
<td>• Inferior virologic efficacy</td>
</tr>
<tr>
<td>ABC/3TC/ZDV + TDF As quadruple-NRTI combination regimen</td>
<td>• Inferior virologic efficacy</td>
</tr>
<tr>
<td>d4T + 3TC</td>
<td>• Significant toxicities (including lipoatrophy, peripheral neuropathy and hyperlactatemia (including symptomatic and life-threatening lactic acidosis, hepatic steatosis, and pancreatitis)</td>
</tr>
</tbody>
</table>
| ddI + 3TC (or FTC) | • Inferior virologic efficacy  
• Limited clinical trial experience in ART-naive patients  
• ddI toxicities such as pancreatitis and peripheral neuropathy |
| ddI + TDF | • High rate of early virologic failure  
• Rapid selection of resistance mutations  
• Potential for immunologic nonresponse/CD4 cell decline  
• Increased ddI drug exposure and toxicities |
| ZDV/3TC | • Greater toxicities (including bone marrow suppression, GI toxicities, skeletal muscle myopathy, cardiomyopathy, and mitochondrial toxicities such as lipoatrophy, lactic acidosis, and hepatic steatosis) than recommended NRTIs |
| **NNRTIs**              |                                                 |
| DLV | • Inferior virologic efficacy  
• Inconvenient (three times daily) dosing |
| ETR | • Insufficient data in ART-naive patients |
| NVP | • Associated with serious and potentially fatal toxicity (hepatic events and severe rash, including SJS and TEN)  
• When compared to EFV, NVP did not meet noninferiority criteria |
| **PIs**                 |                                                 |
| ATV (Unboosted) | • Less potent than boosted ATV |
| DRV (Unboosted) | • Use without RTV or COBI has not been studied |
| FPV (Unboosted) or FPV/r | • Virologic failure with unboosted FPV-based regimen may result in selection of mutations that confer resistance to FPV and DRV  
• Less clinical trial data for FPV/r than for other RTV-boosted PIs |
| IDV (Unboosted) | • Inconvenient dosing (three times daily with meal restrictions)  
• Fluid requirement  
• IDV toxicities such as nephrolithiasis and crystalluria |
| IDV/r | • Fluid requirement  
• IDV toxicities such as nephrolithiasis and crystalluria |
| LPV/r + 2 NRTIs | • Higher pill burden than other PI-based regimens  
• Higher ritonavir dose than other PI-based regimens  
• GI intolerance |
| NFV | • Inferior virologic efficacy  
• Diarrhea |
| RTV as sole PI | • High pill burden  
• GI intolerance  
• Metabolic toxicity |
<table>
<thead>
<tr>
<th>ARV Components or Regimens</th>
<th>Reasons for Not Recommending as Initial Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PIs, continued</strong></td>
<td></td>
</tr>
<tr>
<td>SQV (Unboosted)</td>
<td>• Inadequate bioavailability</td>
</tr>
<tr>
<td></td>
<td>• Inferior virologic efficacy</td>
</tr>
<tr>
<td>SQV/r</td>
<td>• High pill burden</td>
</tr>
<tr>
<td></td>
<td>• Can cause QT and PR prolongation; requires pretreatment and follow-up ECG</td>
</tr>
<tr>
<td>TPV/r</td>
<td>• Inferior virologic efficacy</td>
</tr>
<tr>
<td></td>
<td>• Higher rate of adverse events than other RTV-boosted PIs</td>
</tr>
<tr>
<td></td>
<td>• Higher dose of RTV required for boosting than other RTV-boosted PIs</td>
</tr>
<tr>
<td><strong>CCR5 Antagonist</strong></td>
<td></td>
</tr>
<tr>
<td>MVC</td>
<td>• Requires testing for CCR5 tropism before initiation of therapy</td>
</tr>
<tr>
<td></td>
<td>• No virologic benefit when compared with other recommended regimens</td>
</tr>
<tr>
<td></td>
<td>• Requires twice-daily dosing</td>
</tr>
</tbody>
</table>

**Key to Acronyms:** 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; CD4 = CD4 T lymphocyte; COBI or c = cobicistat; d4T = stavudine; ddl = didanosine; DLV = delavirdine; DRV = darunavir; ECG = electrocardiogram; EFV = efavirenz; ETR = etravirine; FPV = fosamprenavir; FTC = emtricitabine; GI = gastrointestinal; IDV = indinavir; LPV = lopinavir; MVC = maraviroc; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; RTV or r = ritonavir; SJS = Stevens Johnson Syndrome; SQV = saquinavir; TDF = tenofovir disoproxil fumarate; TEN = toxic epidermal necrolysis; TPV = tipranavir; ZDV = zidovudine
### Table 10. Antiretroviral Options for Patients with Virologic Failure (page 1 of 2)

Designing a new regimen for patients with treatment failure should always be guided by results from current and past resistance testing and ARV history. This table summarizes the text above and displays the most common or likely clinical scenarios seen in patients with virologic failure. It is also crucial to provide continuous adherence support to all patients before and after regimen changes. For more detailed descriptions, please refer to the text above and/or consult an expert in drug resistance to assist in the design of a new regimen.

<table>
<thead>
<tr>
<th>Clinical Scenario</th>
<th>Type of Failing Regimen</th>
<th>Resistance Considerations</th>
<th>New Regimen Options</th>
<th>Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Regimen Failure</td>
<td>NNRTI + 2 NRTIs</td>
<td>Most likely resistant to NNRTI +/- 3TC/FTC (i.e., NNRTI mutations +/- M184V/I, without resistance to other NRTIs)</td>
<td>• Boosted PI + 2 NRTIs (at least 1 active) (AIII); or • INSTI + 2 NRTIs (if only 1 of the NRTIs is fully active, or if adherence is a concern, DTG is preferred over EVG or RAL) (AIII); or • Boosted PI + INSTI (AIII)</td>
<td>Resuppression</td>
</tr>
<tr>
<td></td>
<td>Boosted PI + 2 NRTIs</td>
<td>Most likely no resistance or resistance only to 3TC/FTC (i.e., M184V/I, without resistance to other NRTIs)</td>
<td>• Continue same regimen (AII); or • Another boosted PI + 2 NRTIs (at least 1 active) (AII); or • INSTI + 2 NRTIs (at least 1 active) (if only 1 of the NRTIs is fully active, or if adherence is a concern, DTG is preferred over EVG or RAL) (AIII); or • Boosted PI + INSTI (BIII)</td>
<td>Resuppression</td>
</tr>
<tr>
<td></td>
<td>INSTI + 2 NRTIs</td>
<td>3TC/FTC (i.e., only M184V/I, without resistance to other NRTIs)</td>
<td>• Boosted PI + 2 NRTIs (at least 1 active) (AIII); or • DTG + 2 NRTIs (at least 1 active) (AIII); or • Boosted PI + INSTI (BIII)</td>
<td>Resuppression</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No INSTI resistance</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Resistance to first-line DTG is rare</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>EVG or RAL +/- 3TC/FTC (i.e., INSTI mutations +/- M184V/I, without resistance to other NRTIs)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Resistance to first-line DTG is rare</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Second Regimen Failure and Beyond</td>
<td>Drug resistance with active treatment options</td>
<td>Use past and current genotypic +/- phenotypic resistance testing and ART history in designing new regimen</td>
<td>• At least 2, and preferably 3, fully active agents (AI) • Partially active drugs may be used if no other options are available • Consider using ARV with a different mechanism of action</td>
<td>Resuppression</td>
</tr>
</tbody>
</table>
### Second Regimen Failure and Beyond, continued

- **Multiple or extensive drug resistance with few treatment options**
  - Use past and current genotypic and phenotypic resistance testing to guide therapy
  - Consider viral tropism assay if use of maraviroc is considered
  - Consult an expert in drug resistance, if needed
  - Identify as many active or partially active drugs as possible based on resistance testing results
  - Consider using ARV with a different mechanism of action
  - Consider enrollment into clinical trials or expanded access programs for investigational agents, if available
  - Discontinuation of ARVs is not recommended

### Previously Treated Patients with Suspected Drug Resistance, but Limited or Incomplete ART and Resistance History

- **Unknown**
  - Obtain medical records if possible
  - Resistance testing may be helpful in identifying prior drug resistance, even if the patient has been off ART, keeping in mind that resistance mutations may not be detected in the absence of drug pressure.
  - Consider restarting the old regimen, and obtain viral load and resistance testing 2-4 weeks after reintroduction of therapy
  - If there is no available ARV history, consider initiating a regimen with drugs with high genetic barrier to resistance (e.g., DTG and/or boosted DRV)

### Resuppression, if possible; otherwise, keep viral load as low as possible and CD4 cell count as high as possible

<table>
<thead>
<tr>
<th>Clinical Scenario</th>
<th>Type of Failing Regimen</th>
<th>Resistance Considerations</th>
<th>New Regimen Options</th>
<th>Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previously Treated Patients with Suspected Drug Resistance, but Limited or Incomplete ART and Resistance History</td>
<td>Unknown</td>
<td>Obtain medical records if possible</td>
<td>• Consider restarting the old regimen, and obtain viral load and resistance testing 2-4 weeks after reintroduction of therapy</td>
<td>Resuppression</td>
</tr>
</tbody>
</table>

---

**Table 10. Antiretroviral Options for Patients with Virologic Failure** (page 2 of 2)

<table>
<thead>
<tr>
<th>Clinical Scenario</th>
<th>Type of Failing Regimen</th>
<th>Resistance Considerations</th>
<th>New Regimen Options</th>
<th>Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Second Regimen Failure and Beyond, continued</td>
<td>Multiple or extensive drug resistance with few treatment options</td>
<td>Use past and current genotypic and phenotypic resistance testing to guide therapy Consider viral tropism assay if use of maraviroc is considered Consult an expert in drug resistance, if needed</td>
<td>• Identify as many active or partially active drugs as possible based on resistance testing results Consider using ARV with a different mechanism of action Consider enrollment into clinical trials or expanded access programs for investigational agents, if available Discontinuation of ARVs is not recommended</td>
<td>Resuppression, if possible; otherwise, keep viral load as low as possible and CD4 cell count as high as possible</td>
</tr>
</tbody>
</table>

---

*1 There are insufficient data to provide a recommendation for the continuation of 3TC/FTC in the presence of M184V/I.

2 When switching an ARV regimen in a patient with HIV/HBV coinfection, ARV drugs active against HBV should be continued as part of the new regimen. Discontinuation of these drugs may cause serious hepatocellular damage resulting from reactivation of HBV.

3 If other NRTI resistance mutations are present, use resistance testing results to guide NRTI usage in the new regimen.

4 Response to DTG depends on the type and number of INSTI mutations.

**Key to Acronyms:** 3TC = lamivudine; ART = antiretroviral therapy; ARV = antiretroviral; CD4 = CD4 T lymphocyte; DRV = darunavir; DTG = dolutegravir; EVG = elvitegravir; FTC = emtricitabine; HBV = hepatitis B virus; INSTI = integrase strand transfer inhibitor; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; RAL = raltegravir
Table 11. Identifying, Diagnosing, and Managing Acute and Recent HIV-1 Infection

Suspicion of Acute HIV-1 Infection:

• Acute HIV-1 infection should be considered in individuals with signs or symptoms described below and recent (within 2 to 6 weeks) high risk of exposure to HIV-1.\(^a\)

• Signs, symptoms, or laboratory findings of acute HIV-1 infection may include but are not limited to one or more of the following: fever, lymphadenopathy, skin rash, myalgia, arthralgia, headache, diarrhea, oral ulcers, leucopenia, thrombocytopenia, transaminase elevation.

• High-risk exposures include sexual contact with a person who has HIV-1 infection or a person at risk of HIV-1 infection, sharing of injection drug use paraphernalia, or any exposure in which an individual’s mucous membranes or breaks in the skin come in contact with bodily fluid potentially infected with HIV.

• Differential diagnosis: The differential diagnosis of HIV-1 infection may include but is not limited to viral illnesses such as Epstein-Barr virus (EBV) and non-EBV (e.g., cytomegalovirus) infectious mononucleosis syndromes, influenza, viral hepatitis, streptococcal infection, or syphilis.

Evaluation/Diagnosis of Acute HIV-1 Infection:

• Acute HIV-1 infection is defined as detectable HIV-1 RNA or p24 antigen (the antigen used in currently available HIV antigen/antibody [Ag/Ab] combination assays) in the setting of a negative or indeterminate HIV-1 antibody test result.

• A reactive HIV antibody test result or Ag/Ab combination test result must be followed by supplemental confirmatory testing.

• A negative or indeterminate HIV-1 antibody test result in a person with a reactive Ag/Ab test result or in whom acute HIV-1 infection is suspected requires plasma HIV-1 RNA testing to diagnose acute HIV-1 infection.

• A positive result on a quantitative or qualitative plasma HIV-1 RNA test in the setting of a negative or indeterminate antibody test result indicates that acute HIV-1 infection is highly likely, in which case, the diagnosis of HIV-1 infection should be later confirmed by subsequent documentation of HIV antibody seroconversion.

Antiretroviral Therapy After Diagnosis of Early HIV-1 Infection:

• ART is recommended for all individuals with HIV (AI), and should be offered to all patients with early HIV-1 infection.

• All pregnant women with early HIV-1 infection should begin ART as soon as possible for their health and to prevent perinatal transmission of HIV-1 (AI).

• A blood sample for genotypic drug resistance testing should be obtained before initiation of ART to guide the selection of the regimen (AII), but the initiation of ART should be done as soon as possible, often prior to availability of resistance test results. If resistance is subsequently identified, treatment should be modified appropriately.

• If no resistance data are available, then a pharmacologically boosted PI-based regimen is recommended because resistance to PIs emerges slowly and clinically significant transmitted resistance to PIs is uncommon. Boosted DRV (DRV/r or DRV/c) plus FTC and either TDF or TAF is a recommended regimen in this setting (AIII). For similar reasons, DTG plus FTC and either TDF or TAF are reasonable options although the data regarding transmission of INSTI-resistant HIV and the efficacy of this regimen in early HIV infection are limited (AIII).

• In patients without transmitted drug-resistant virus, ART should be initiated with one of the combination regimens recommended for patients with chronic HIV-1 infection (see What to Start) (AIII).

\(^a\) In some settings, behaviors that increase the risk of HIV-1 infection may not be recognized or perceived as risky by the health care provider or the patient, or both. Thus, even in the absence of reported high-risk behaviors, symptoms and signs consistent with acute retroviral syndrome should motivate practitioners to consider a diagnosis of acute HIV-1 infection.

Key to Acronyms: ART = antiretroviral therapy; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; FTC = emtricitabine; INSTI = integrase strand transfer inhibitor; PI = protease inhibitor; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate
Table 12. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of HCV in Adults with HIV (page 1 of 4)

The recommendations in this table for concomitant use of selected HIV drugs with Food and Drug Administration (FDA)-approved hepatitis C virus (HCV) direct-acting antiviral (DAA) drugs are based on available pharmacokinetic interaction data or predictions based on the known metabolic pathway of the agents. In some cases, there are not enough data to make any recommendations, and these instances are indicated in the table. In all cases where HIV and HCV drugs are used concomitantly, patients should be closely monitored for HIV and HCV virologic efficacy and potential toxicities. As the field of HCV therapy is rapidly evolving, readers should also refer to the latest drug product labels and HCV guidelines (www.hcvguidelines.org) for updated information.

Note: Interactions with fosamprenavir, indinavir, nelfinavir, and saquinavir are not included in this table. Please refer to the FDA product labels for information regarding drug interactions with these HIV protease inhibitors (PIs). Because the HCV PIs boceprevir and telaprevir are no longer recommended for HCV treatment, these products have been removed from this table.

<table>
<thead>
<tr>
<th>Selected HIV Drugs</th>
<th>Coformulated</th>
<th>HCV Direct-Acting Antiviral Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NS5A/NS5B Inhibitor</td>
<td>NS5A/NS5B Inhibitor/ NS3/4A Protease Inhibitor</td>
</tr>
<tr>
<td>Daclatasvir</td>
<td>☑</td>
<td>☑</td>
</tr>
<tr>
<td>Sofosbuvir</td>
<td>☑</td>
<td>☑</td>
</tr>
<tr>
<td>Ledipasvir/ Sofosbuvir</td>
<td>☑</td>
<td>☑</td>
</tr>
<tr>
<td>Sofosbuvir/ Velpatasvir</td>
<td>☑</td>
<td>☑</td>
</tr>
<tr>
<td>Sofosbuvir/ Velpatasvir/ Voxilaprevir</td>
<td>☑</td>
<td>☑</td>
</tr>
<tr>
<td>Glecaprevir/ Pibrentasvir</td>
<td>☑</td>
<td>☑</td>
</tr>
<tr>
<td>Elbasvir/ Grazoprevir</td>
<td>☑</td>
<td>☑</td>
</tr>
<tr>
<td>Ombitasvir/ Paritaprevir/ Ritonavir plus Dasabuvir</td>
<td>☑</td>
<td>☑</td>
</tr>
<tr>
<td>Simprevir</td>
<td>☑</td>
<td>☑</td>
</tr>
</tbody>
</table>

NRTIs

| 3TC | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ |
| ABC | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ |
| FTC | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ |
| TDF | ☑ | ☑ | Monitor for TDF toxicity. | ☑ | Monitor for TDF toxicity. | ☑ | Monitor for TDF toxicity. |
| TAF | ☑ | ☑ | ☑ | ☑ | ☑ | ☑ |

PIs

| Unboosted ATV | ☑ | ☑ | ☑ | X | X | X | ☑ |

Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents

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Table 12. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of HCV in Adults with HIV (page 2 of 4)

<table>
<thead>
<tr>
<th>Selected HIV Drugs</th>
<th>HCV Direct-Acting Antiviral Agents</th>
<th>Coformulated</th>
<th>SHOULD NOT BE USED IN THOSE WITH MODERATE TO SEVERE HEPATIC IMPAIRMENT (Cirrhosis classified as Child-Turcotte Pugh class B or C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NS5A Inhibitor</td>
<td>NS5B Inhibitor</td>
<td>NS5A/NS5B Inhibitor</td>
<td>NS5A/NS5B Inhibitor/ NS3/4A Protease Inhibitor</td>
</tr>
<tr>
<td>Daclatasvir</td>
<td>Sofosbuvir</td>
<td>Ledipasvir/ Sofosbuvir</td>
<td>Sofosbuvir/Velpatasvir</td>
</tr>
</tbody>
</table>

PIs, continued

<table>
<thead>
<tr>
<th>ATV/r or ATV/c</th>
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<tr>
<td>TPV/r</td>
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NNRTIs

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</tr>
</tbody>
</table>

Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents

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Table 12. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of HCV in Adults with HIV (page 3 of 4)

<table>
<thead>
<tr>
<th>Selected HIV Drugs</th>
<th>HCV Direct-Acting Antiviral Agents</th>
<th>Coformulated</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td><strong>SHOULD NOT BE USED IN THOSE WITH MODERATE TO SEVERE HEPATIC IMPAIRMENT</strong> (Cirrhosis classified as Child-Turcotte Pugh class B or C)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>NS5A Inhibitor</strong></td>
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<td></td>
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<tr>
<td><strong>NS5B Inhibitor</strong></td>
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<td></td>
</tr>
<tr>
<td>NS5A/NS5B Inhibitor</td>
<td>NS5A/NS5B Inhibitor/NS3A/4A Protease Inhibitor</td>
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<tr>
<td></td>
<td>NS5A/NS5B Inhibitor/NS3/4A Protease Inhibitor</td>
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</tr>
<tr>
<td></td>
<td>NS5A/NS5B Inhibitor/NS3/4A Protease Inhibitor plus NS5B Inhibitor</td>
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</tr>
<tr>
<td></td>
<td>NS3A/4A Protease Inhibitora</td>
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</tr>
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</table>

**INSTIs**

<table>
<thead>
<tr>
<th>INSTIs</th>
<th>DTG</th>
<th>EVG/c/TDF/FTC</th>
<th>EVG/c/TAF/FTC</th>
<th>RAL</th>
<th>CCR5 Antagonist</th>
</tr>
</thead>
<tbody>
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<tr>
<td></td>
<td>✔</td>
<td>🔻 DCV dose to 30 mg/day</td>
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<tr>
<td></td>
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<td>🔻 DCV dose to 30 mg/day</td>
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<td>✔</td>
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</tr>
</tbody>
</table>

**Notes:**
- Dasabuvir must be prescribed with ombitasvir/paritaprevir/ritonavir
- Reduce ATV dose to 300 mg and take in the morning at same time as ombitasvir/paritaprevir/ritonavir plus dasabuvir. If RTV cannot be used, choose an alternative HCV regimen.
- Take ATV 300 mg in the morning at same time as ombitasvir/paritaprevir/ritonavir plus dasabuvir. If taking RTV or COBI, discontinue RTV or COBI in HIV regimen until HCV therapy is completed.

Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents

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Table 12. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of HCV in Adults with HIV  (page 4 of 4)

Consider alternative HCV or ART to avoid increases in TDF exposure. If co-administration is necessary, monitor patient for TDF-associated adverse reactions.

Due to increased voxilaprevir exposures when given with pharmacologically boosted DRV or EVG, monitoring patients for hepatotoxicity is recommended until more safety data in clinical settings becomes available.

Due to increased glecaprevir exposures when given with EVG/c, monitoring patients for hepatotoxicity is recommended until more safety data in clinical settings becomes available.

Key to Symbols:

✔ = ARV agents that can be used concomitantly
✘ = ARV agents not recommended
?
= data limited or not available on pharmacokinetic interactions with ARV drug

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/r = atazanavir/ritonavir; ATV/c = atazanavir/cobicistat; COBI = cobicistat; DAA = direct-acting antiviral agents; DRV = darunavir; DRV/r = darunavir/ritonavir; DRV/c = darunavir/cobicistat; DTG = dolutegravir; DSV = dasabuvir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; HCV = hepatitis C virus; INSTI = integrase strand transfer inhibitor; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PI/c = cobicistat-boosted protease inhibitor; PI/r = ritonavir-boosted protease inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV/r = tipranavir/ritonavir
Table 13. Strategies to Improve Linkage to Care, Retention in Care, Adherence to Appointments, and Adherence to Antiretroviral Therapy (page 1 of 2)

<table>
<thead>
<tr>
<th>Strategies</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Provide an accessible, trustworthy, nonjudgmental multidisciplinary health</td>
<td>• Care providers, nurses, social workers, case managers, pharmacists, and medication managers.</td>
</tr>
<tr>
<td>care team.</td>
<td></td>
</tr>
<tr>
<td>Strengthen early linkage to care and retention in care.</td>
<td>• Encourage health care team participation in linkage to and retention in care.</td>
</tr>
<tr>
<td>• Use ARTAS training (if available).</td>
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</tr>
<tr>
<td>Evaluate patient’s knowledge about HIV infection, prevention, and treatment</td>
<td>• Keeping the patient’s current knowledge base in mind, provide information about HIV, including the natural history of the disease, HIV viral load and CD4 count and expected clinical outcomes according to these parameters, therapeutic and prevention consequences of poor adherence, and importance of staying in HIV care.</td>
</tr>
<tr>
<td>and assessment, and, based on this assessment, provide HIV-related</td>
<td></td>
</tr>
<tr>
<td>information.</td>
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</tr>
<tr>
<td>Identify facilitators, potential barriers to adherence, and necessary</td>
<td>• Assess patient’s cognitive competence and impairment.</td>
</tr>
<tr>
<td>medication management skills both before starting ART and on an ongoing</td>
<td>• Assess behavioral and psychosocial challenges, including depression, mental illnesses, levels of social support, levels of alcohol consumption and current substance use, nondisclosure of HIV serostatus, and stigma.</td>
</tr>
<tr>
<td>basis.</td>
<td>• Identify and address language and literacy barriers.</td>
</tr>
<tr>
<td>• Assess beliefs, perceptions, and expectations about taking ART (e.g.,</td>
<td>• Assess structural issues, including unstable housing, lack of income, unpredictable daily schedule, lack of prescription drug coverage, lack of continuous access to medications, transportation problems.</td>
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<tr>
<td>impact on health, side effects, disclosure issues, consequences of poor</td>
<td></td>
</tr>
<tr>
<td>adherence).</td>
<td></td>
</tr>
<tr>
<td>• Ask about medication-taking skills and foreseeable challenges with</td>
<td></td>
</tr>
<tr>
<td>adherence (e.g., past difficulty keeping appointments, adverse effects</td>
<td></td>
</tr>
<tr>
<td>from previous medications, issues managing other chronic medications,</td>
<td></td>
</tr>
<tr>
<td>need for medication reminders and organizers).</td>
<td></td>
</tr>
<tr>
<td>• Assess structural issues, including unstable housing, lack of income,</td>
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<tr>
<td>unpredictable daily schedule, lack of prescription drug coverage, lack</td>
<td></td>
</tr>
<tr>
<td>of continuous access to medications, transportation problems.</td>
<td></td>
</tr>
<tr>
<td>Provide needed resources.</td>
<td>• Provide or refer for mental health and/or substance abuse treatment.</td>
</tr>
<tr>
<td>• Provide resources to obtain prescription drug coverage (e.g., Common</td>
<td>• Provide resources about stable housing, social support, transportation assistance, and income and food security.</td>
</tr>
<tr>
<td>Pharmaceutical Company HIV Patient Assistance Programs and Cost-Sharing</td>
<td></td>
</tr>
<tr>
<td>Assistance Programs: <a href="http://bit.ly/1XIahvN">http://bit.ly/1XIahvN</a></td>
<td></td>
</tr>
<tr>
<td>Involve the patient in ARV regimen selection.</td>
<td>• Review potential side effects, dosing frequency, pill burden, storage requirements, food requirements, and consequences of poor adherence.</td>
</tr>
<tr>
<td>• Assess daily activities and tailor regimen to predictable and routine</td>
<td>• Consider preferential use of PI/r-based or DTG-based ART if poor adherence is anticipated.</td>
</tr>
<tr>
<td>daily events.</td>
<td>• Consider use of STR formulations.</td>
</tr>
<tr>
<td>• Assess structural issues, including unstable housing, lack of income,</td>
<td>• Assess if cost/copayment for drugs will affect adherence and access to medications.</td>
</tr>
<tr>
<td>unpredictable daily schedule, lack of prescription drug coverage, lack</td>
<td></td>
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<tr>
<td>of continuous access to medications.</td>
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<tr>
<td>Assess adherence at every clinic visit.</td>
<td>• Monitor viral load as a strong biologic measure of adherence.</td>
</tr>
<tr>
<td>• Use a simple behavioral rating scale or self-reported assessment.</td>
<td>• Employ a structured format that normalizes or assumes less-than-perfect adherence and minimizes socially desirable or “white-coat adherence” responses.</td>
</tr>
<tr>
<td>• Ensure that other members of the health care team also assess and</td>
<td>• Ensure that other members of the health care team also assess and support adherence.</td>
</tr>
<tr>
<td>support adherence.</td>
<td></td>
</tr>
<tr>
<td>Use positive reinforcement to foster adherence success.</td>
<td>• Inform patients of low or nondetectable levels of HIV viral load and increases in CD4 cell counts.</td>
</tr>
<tr>
<td>• Thank patients for attending their appointments.</td>
<td></td>
</tr>
</tbody>
</table>
Table 13. Strategies to Improve Linkage to Care, Retention in Care, Adherence to Appointments, and Adherence to Antiretroviral Therapy (page 2 of 2)

<table>
<thead>
<tr>
<th>Strategies</th>
<th>Examples</th>
</tr>
</thead>
</table>
| Identify the type of and reasons for poor adherence and target ways to improve adherence. | • Failure to understand dosing instructions.  
• Complexity of regimen (e.g., pill burden, size, dosing schedule, food requirements, polypharmacy).  
• Pill aversion or pill fatigue.  
• Adverse effects.  
• Inadequate understanding of drug resistance and its relationship to adherence.  
• Patient is unaware of appointments or appointments are not scheduled with proper patient input.  
• Cost-related issues (copays for medications or visits, missed work time).  
• Depression, drug and alcohol use, homelessness, poverty.  
• Stigma of taking pills or attending HIV-related appointments.  
• Nondisclosure of status leading to missed doses, refills, or appointments. |
| Select from among available effective adherence and retention interventions. | • See [https://www.cdc.gov/hiv/research/interventionresearch/compendium/index.html](https://www.cdc.gov/hiv/research/interventionresearch/compendium/index.html) for a summary of best practice interventions to improve linkage, retention, and adherence.  
• Use adherence-related tools to complement education and counseling interventions (e.g., text messaging, pill box monitors, pill boxes, alarms).  
• Use community resources to support adherence (e.g., visiting nurses, community workers, family, peer advocates, transportation assistance).  
• Use patient prescription assistance programs (see above, under “Provide needed resources”).  
• Use motivational interviews.  
• Provide outreach for patients who drop out of care  
• Use peer or paraprofessional treatment navigators.  
• Recognize positive clinical outcomes resulting from better adherence.  
• Arrange for DOT in persons in substance use treatment (if feasible).  
• Enhance clinic support and structures to promote linkage and retention (reminder calls, flexible scheduling, open access, active referrals, and improved patient satisfaction). |
| Systematically monitor retention in care. | • Record and follow up on missed visits. |

**Key to Acronyms:** ART = antiretroviral therapy; ARTAS = Anti-Retroviral Treatment and Access to Services; ARV = antiretroviral; CD4 = CD4 T lymphocyte; DOT = directly observed therapy; DTG = dolutegravir; PI/r = ritonavir-boosted protease inhibitor; STR = single tablet regimen
Table 14. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy, page 1 of 5

N/A indicates either that there are no reported cases for that particular side effect or that data for the specific ARV drug class are not available. See Appendix B for additional information listed by drug.

<table>
<thead>
<tr>
<th>Adverse Effect</th>
<th>Drug Class</th>
<th>NRTIs</th>
<th>NNRTIs</th>
<th>Pls</th>
<th>INSTIs</th>
<th>EIs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bleeding Events</strong></td>
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<td></td>
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<td>N/A</td>
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<td><strong>Bone Density Effects</strong></td>
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<td>TDF:</td>
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<td>TAF:</td>
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<tr>
<td><strong>Bone Marrow Suppression</strong></td>
<td>ZDV:</td>
<td>N/A</td>
<td>N/A</td>
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<td>N/A</td>
<td>N/A</td>
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<td><strong>Cardiac Conduction Effects</strong></td>
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<td></td>
<td>RPV, EFV:</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
<td>N/A</td>
<td>N/A</td>
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<tr>
<td><strong>Cardiovascular Disease</strong></td>
<td>ABC and ddl:</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
<td>N/A</td>
<td>N/A</td>
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<tr>
<td><strong>Cholelithiasis</strong></td>
<td></td>
<td>N/A</td>
<td>N/A</td>
<td></td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>
### Table 14. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy, page 2 of 5

<table>
<thead>
<tr>
<th>Adverse Effect</th>
<th>Drug Class</th>
<th>NRTIs</th>
<th>NNRTIs</th>
<th>Pls</th>
<th>INSTIs</th>
<th>Els</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diabetes Mellitus and Insulin Resistance</strong></td>
<td></td>
<td></td>
<td></td>
<td>Reported for some (IDV, LPV/r), but not all, Pls.</td>
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<tr>
<td></td>
<td>ZDV, d4T, and ddi</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Dyslipidemia</strong></td>
<td>d4T &gt; ZDV &gt; ABC: ↑ TG and LDL</td>
<td>EFV: ↑TG, ↑LDL, ↑HDL</td>
<td>All RTV- or COBI-boosted Pls: ↑ TG, ↑ LDL, ↑ HDL</td>
<td>EVG/c: ↑ TG, ↑ LDL, ↑ HDL</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TAF: ↑ TG, ↑ LDL, ↑ HDL (no change in TC:HDL ratio)</td>
<td></td>
<td>LPV/r and FPV/r &gt; DRV/r and ATV/r: ↑ TG</td>
<td></td>
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<tr>
<td></td>
<td>TDF has been associated with lower lipid levels than ABC or TAF.</td>
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</tr>
<tr>
<td><strong>Gastrointestinal Effects</strong></td>
<td>ddl and ZDV &gt; other NRTIs: Nausea and vomiting</td>
<td>GI intolerance (e.g., diarrhea, nausea, vomiting)</td>
<td>EVG/c: Nausea and diarrhea</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>ddi: Pancreatitis</td>
<td></td>
<td></td>
<td>N/A</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td><strong>Hepatic Effects</strong></td>
<td>Reported with most NRTIs.</td>
<td>EFV: Fulminant hepatitis progressing to hepatic failure requiring transplantation or death have been reported.</td>
<td>All Pls: Drug-induced hepatitis and hepatic decompensation have been reported; greatest frequency occurs with TPV/r.</td>
<td></td>
<td>MVC: Hepatotoxicity with or without rash or HSRs reported.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ZDV, d4T, or ddi: Steatosis</td>
<td>NVP: Severe hepatotoxicity associated with skin rash or hypersensitivity. Two-week NVP dose escalation may reduce risk. Risk is greater for women with pre-NVP CD4 count &gt;250 cells/mm³ and men with pre-NVP CD4 count &gt;400 cells/mm³. NVP should <strong>never</strong> be used for post-exposure prophylaxis.</td>
<td>TPV/r: <strong>Contraindicated</strong> in patients with hepatic insufficiency (Child Pugh class B or C).</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>ddi: Prolonged exposure linked to noncirrhotic portal hypertension and esophageal varices.</td>
<td>EFV and NVP are <strong>not recommended</strong> in patients with hepatic insufficiency (Child-Pugh class B or C).</td>
<td>IDV, ATV: Jaundice due to indirect hyperbilirubinemia.</td>
<td></td>
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<tr>
<td></td>
<td>When TAF, TDF, 3TC, and FTC are withdrawn in patients with HBV/HIV coinfection or when HBV resistance develops: Patients with HBV/HIV coinfection may develop severe hepatic flares.</td>
<td></td>
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</tr>
</tbody>
</table>

*Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV*

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### Table 14. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy

<table>
<thead>
<tr>
<th>Adverse Effect</th>
<th>NRTIs</th>
<th>NNRTIs</th>
<th>Pls</th>
<th>INSTIs</th>
<th>Els</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hypersensitivity Reaction</strong></td>
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<tr>
<td>Excluding rash alone or Stevens-Johnson syndrome</td>
<td><strong>ABC:</strong> Contraindicated if HLA-B<em>5701-positive. &lt;br&gt; Median onset for HSR is 9 days; 90% of reactions occur within first 6 weeks of treatment. &lt;br&gt; <strong>HSR symptoms (in order of descending frequency):</strong> Fever, rash, malaise, nausea, headache, myalgia, chills, diarrhea, vomiting, abdominal pain, dyspnea, arthralgia, and respiratory symptoms &lt;br&gt; Symptoms worsen with continuation of ABC. &lt;br&gt; Patients should not be rechallenged with ABC if HSR is suspected, regardless of their HLA-B</em>5701 status.</td>
<td>N/A</td>
<td>RAL: HSR reported when RAL is given with other drugs also known to cause HSR. All ARVs should be stopped if HSR occurs. &lt;br&gt; DTG: Reported in &lt;1% of patients in clinical development program.</td>
<td>MVC: HSR reported as part of a syndrome related to hepatotoxicity.</td>
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<tr>
<td><strong>Lactic Acidosis</strong></td>
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<tr>
<td><strong>Reported with NRTIs, especially d4T, ZDV, and ddI:</strong> Insidious onset with GI prodrome, weight loss, and fatigue. May rapidly progress with tachycardia, tachypnea, jaundice, weakness, mental status changes, pancreatitis, and organ failure. Mortality high if serum lactate &gt;10 mmol/L. &lt;br&gt; Women and obese patients at increased risk.</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
</tr>
</tbody>
</table>
### Table 14. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy, page 4 of 5

<table>
<thead>
<tr>
<th>Adverse Effect</th>
<th>NRTIs</th>
<th>NNRTIs</th>
<th>PIs</th>
<th>INSTIs</th>
<th>Els</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lipodystrophy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>N/A</td>
</tr>
<tr>
<td>Lipodystrophy: <strong>d4T &gt; ZDV.</strong> More likely when NRTIs are coadministered with EFV than with an RTV-boosted PI.</td>
<td></td>
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<td>N/A</td>
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<tr>
<td>Lipohypertrophy: Trunk fat increase observed with EFV-, PI-, and RAL-containing regimens; however, causal relationship has not been established.</td>
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<td>N/A</td>
</tr>
<tr>
<td><strong>Myopathy/ Elevated Creatine Phosphokinase</strong></td>
<td>ZDV: Myopathy</td>
<td>N/A</td>
<td>N/A</td>
<td>RAL, DTG: ↑ CPK, rhabdomyolysis, and myopathy or myositis have been reported.</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Nervous System/ Psychiatric Effects</strong></td>
<td></td>
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<td>N/A</td>
</tr>
<tr>
<td>d4T &gt; ddI: Peripheral neuropathy (can be irreversible)</td>
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<td>N/A</td>
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<tr>
<td>d4T: Associated with rapidly progressive, ascending neuromuscular weakness resembling Guillain-Barré syndrome (rare).</td>
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<td>N/A</td>
</tr>
<tr>
<td><strong>EFV:</strong> Somnolence, insomnia, abnormal dreams, dizziness, impaired concentration, depression, psychosis, and suicidal ideation. Symptoms usually subside or diminish after 2 to 4 weeks. Bedtime dosing may reduce symptoms. Risk factors include presence of psychiatric illness, concomitant use of agents with neuropsychiatric effects, and increased EFV concentrations because of genetic factors or increased absorption with food. An association between EFV and suicidal ideation, suicide, and attempted suicide was found in a retrospective analysis of comparative trials.</td>
<td></td>
<td></td>
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<td>N/A</td>
</tr>
<tr>
<td><strong>RPV:</strong> Depression, suicidality, sleep disturbances</td>
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<td></td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Rash</strong></td>
<td>FTC: Hyperpigmentation</td>
<td>All NNRTIs</td>
<td>ATV, DRV, FPV, LPV/r, TPV</td>
<td>All INSTIs</td>
<td>MVC</td>
</tr>
</tbody>
</table>
### Table 14. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy, page 5 of 5

<table>
<thead>
<tr>
<th>Adverse Effect</th>
<th>Drug Class</th>
<th>NRTIs</th>
<th>NNRTIs</th>
<th>Pls</th>
<th>INSTIs</th>
<th>Els</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal Effects/ Urolithiasis</td>
<td>TDF: ↑ SCR, proteinuria, hypophosphatemia, urinary phosphate wasting, glycosuria, hypokalemia, and non-anion gap metabolic acidosis. Concurrent use of TDF with COBI- or RTV-containing regimens appears to increase risk. TAF: Less impact on renal biomarkers and lower rates of proteinuria than TDF.</td>
<td><strong>RPV</strong>: Inhibits Cr secretion without reducing renal glomerular function.</td>
<td>ATV and LPV/r: Increased risk of chronic kidney disease in a large cohort study. IDV: ↑ SCR, pyuria, renal atrophy, or hydronephrosis IDV, ATV: Stone or crystal formation. Adequate hydration may reduce risk.</td>
<td><strong>COBI</strong> (as a boosting agent for DRV or ATV): Inhibits Cr secretion without reducing renal glomerular function.</td>
<td>DTG and COBI (as a boosting agent for EVG): Inhibits Cr secretion without reducing renal glomerular function.</td>
<td>N/A</td>
</tr>
<tr>
<td>Stevens-Johnson Syndrome/ Toxic Epidermal Necrosis</td>
<td>Some reported cases for ddI and ZDV.</td>
<td><strong>NVP &gt; DLV, EFV, ETR, RPV</strong></td>
<td>Some reported cases for FPV, DRV, IDV, LPV/r, and ATV.</td>
<td>RAL</td>
<td>N/A</td>
<td></td>
</tr>
</tbody>
</table>

**Key to Abbreviations:**
- 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/r = atazanavir/ritonavir; BMD = bone mineral density; CD4 = CD4 T lymphocyte; Cr = creatinine; CNS = central nervous system; COBI = cobicistat; CPK = creatine phosphokinase; CVD = cardiovascular disease; d4T = stavudine; ddC = zalcitabine; ddI = didanosine; DLV = delavirdine; DRV = darunavir;DRV/r = darunavir/ritonavir; DTG = dolutegravir; ECG = electrocardiogram; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; FPV = fosamprenavir; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; GI = gastrointestinal; HBV = hepatitis B virus; HDL = high-density lipoprotein; HSR = hypersensitivity reaction; IDV = indinavir; INSTI = integrase strand transfer inhibitor; LDL = low-density lipoprotein; LPV/r = lopinavir/ritonavir; MI = myocardial infarction; MVC = maraviroc; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SCR = serum creatinine; SQV = saquinavir; SQV/r = saquinavir/ritonavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TG = triglyceride; TPV = tipranavir; TPV/r = tipranavir/ritonavir; ZDV = zidovudine
### Table 15. Antiretroviral Therapy-Associated Adverse Events That Can Be Managed with Substitution of Alternative Antiretroviral Agent

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>ARV Agent(s) or Drug Class</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bone Density Effects</strong></td>
<td>TDF&lt;sup&gt;a&lt;/sup&gt;</td>
<td>ABC&lt;sup&gt;c&lt;/sup&gt; or TAF NRTI-sparing regimens or regimens using only 3TC or FTC as the NRTI may be considered, if appropriate. Declines in BMD have been observed upon initiation of most ART regimens. Switching from TDF to alternative ARV agents has been shown to increase bone density, but the clinical significance of this increase remains uncertain. TAF is associated with smaller declines in BMD than TDF, and patients show improvement in BMD upon switching to TAF. The long-term impact of TAF on patients with osteopenia or osteoporosis is unknown; close clinical monitoring is recommended in this setting.</td>
</tr>
<tr>
<td><strong>Bone Marrow Suppression</strong></td>
<td>ZDV</td>
<td>TDF, TAF, or ABC&lt;sup&gt;c&lt;/sup&gt; ZDV has been associated with neutropenia and macrocytic anemia.</td>
</tr>
<tr>
<td><strong>Cardiac QTc Interval Prolongation</strong></td>
<td>EFV, RPV</td>
<td>A PI- or INSTI-based regimen High EFV and RPV exposures may cause QT prolongation. Consider switching from EFV- or RPV-based regimens if patient is taking other medications with known risk of torsades de pointes, or in patients at higher risk of torsades de pointes.</td>
</tr>
<tr>
<td><strong>Cardiovascular Events</strong></td>
<td>ABC</td>
<td>TDF, TAF, FTC, 3TC ABC use has been associated with cardiovascular disease and cardiac events in some, but not all, observational studies. TDF has been associated with lower lipid levels than TAF.</td>
</tr>
<tr>
<td>Myocardial infarction, ischemic stroke</td>
<td>RTV- or COBI-boosted PI regimens, EFV, EVG/c</td>
<td>RAL, DTG, RPV RAL, DTG, and RPV have less effect on lipids. Large observation cohorts have found an association between some PIs (DRV, FPV, IDV, LPV/r) and an increased risk of CV events. However, this association has not been seen with ATV. Further study is needed.</td>
</tr>
<tr>
<td><strong>Central Nervous System, Neuropsychiatric Side Effects</strong></td>
<td>EFV, RPV</td>
<td>ETR or a PI/c or PI/r INSTIs may be considered with monitoring (see Comments column). In most patients, EFV-related CNS effects subside within 4 weeks after initiation of the drug. Persistent or intolerable effects should prompt substitution of EFV. INSTIs are associated with insomnia. Depression and suicidal ideality have been infrequently reported with INSTI use, primarily in patients with pre-existing psychiatric conditions.</td>
</tr>
<tr>
<td><strong>Dyslipidemia</strong></td>
<td>RTV- or COBI-boosted regimens, EFV, EVG/c</td>
<td>RAL, DTG, RPV Elevated TG and LDL levels are more common with LPV/r and FPV/r than with other RTV-boosted PIs. Improvements in TG and LDL levels have been observed with switch from LPV/r to ATV or ATV/r.&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Includes TDF, FTC, FTC/emtricitabine (FTC/abacavir (ABC)).

<sup>c</sup> Includes TAF, FTC, FTC/emtricitabine (FTC/abacavir (ABC)).
Table 15. Antiretroviral Therapy-Associated Adverse Events That Can Be Managed with Substitution of Alternative Antiretroviral Agent (page 2 of 3)

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>ARV Agent(s) or Drug Class</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gastrointestinal Effects</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea, diarrhea</td>
<td>LPV/r</td>
<td>GI intolerance is common with boosted PIs and is linked to the total dose of RTV. More GI toxicity is seen with LPV/r than with ATV/r or DRV/r. GI effects are often transient, and do not warrant substitution unless persistent and intolerable.</td>
</tr>
<tr>
<td>Other RTV- or COBI-boosted regimens</td>
<td>RAL, DTG, NNRTIs</td>
<td>In a trial of treatment-naive patients, rates of diarrhea and nausea were similar for EVG/c/ TDF/FTC and ATV/r plus TDF/FTC.</td>
</tr>
<tr>
<td><strong>Hypersensitivity Reaction</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABC</td>
<td>TDF or TAF</td>
<td>Never rechallenge with ABC following a suspected HSR, regardless of the patient’s HLA-B*5701 status.</td>
</tr>
<tr>
<td>NVP, EFV, ETR, RPV</td>
<td>Non-NNRTI ART</td>
<td>Risk of HSR with NVP is higher for women and those with high CD4 cell counts.</td>
</tr>
<tr>
<td>DTG, RAL</td>
<td>Non-INSTI ART</td>
<td>Reactions to NVP, ETR, RAL, DTG, and MVC may be accompanied by elevated liver transaminases.</td>
</tr>
<tr>
<td>MVC</td>
<td>Suitable alternative ART</td>
<td></td>
</tr>
<tr>
<td><strong>Insulin Resistance</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LPV/r, FPV/r</td>
<td>INSTI, RPV</td>
<td>Results of switch studies have been inconsistent. Studies in HIV-negative patients suggest a direct causal effect of LPV/r (and IDV) on insulin resistance. However, traditional risk factors may be stronger risk factors for insulin resistance than use of any PI.</td>
</tr>
<tr>
<td><strong>Jaundice and Icterus</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATV, ATV/c, ATV/r</td>
<td>DRV/c, DRV/r, INSTI, or NNRTI</td>
<td>Increases in unconjugated bilirubin are common with ATV and generally do not require modification of therapy unless resultant symptoms are distressing to the patient.</td>
</tr>
<tr>
<td><strong>Lipoatrophy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subcutaneous fat wasting of limbs, face, buttocks</td>
<td>d4T, ZDV</td>
<td>Peripheral lipatrophy is a legacy of prior thymidine analog (d4T and ZDV) use. Switching from these ARVs prevents worsening lipatrophy, but fat recovery is typically slow (may take years) and incomplete.</td>
</tr>
<tr>
<td><strong>Lipohypertrophy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accumulation of visceral, truncal, dorso-cervical, and breast fat has been observed during ART, particularly during use of older PI-based regimens (e.g., IDV), but whether ART directly causes fat accumulation remains unclear. There is no clinical evidence that switching to another first line regimen will reverse weight or visceral fat gain.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Rash</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NNRTIs (especially NVP and EFV)</td>
<td>PI- or INSTI-based regimen</td>
<td>Mild rashes developing after initiation of NNRTIs other than NVP rarely require treatment switch. When serious rash develops due to any NNRTI, switch to another drug class.</td>
</tr>
<tr>
<td>DRV/c, DRV/r</td>
<td>ATVC, ATV/r, or another drug class (e.g., INSTI)</td>
<td>Mild rashes following DRV/r use may resolve with close follow-up only. For more severe reactions, change to an alternative boosted PI or an agent from another drug class.</td>
</tr>
</tbody>
</table>
### Table 15. Antiretroviral Therapy-Associated Adverse Events That Can Be Managed with Substitution of Alternative Antiretroviral Agent  (page 3 of 3)

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>ARV Agent(s) or Drug Class</th>
<th>Switch from</th>
<th>Switch to</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Renal Effects</strong>&lt;br&gt;Including proximal renal tubulopathy and elevated creatinine</td>
<td>TDF&lt;sup&gt;a&lt;/sup&gt;</td>
<td>ABC,&lt;sup&gt;b&lt;/sup&gt; or TAF (for patients with CrCl &gt;30 mL/min), NRTI-sparing regimens, or regimens using only 3TC or FTC as the NRTI may be considered if appropriate.</td>
<td>DTG, RAL, or NNRTI</td>
<td>TDF may cause tubulopathy. Switching from TDF to TAF is associated with improvement in proteinuria and renal biomarkers. The long-term impact of TAF on patients with pre-existing renal disease, including overt proximal tubulopathy, is unknown, and close clinical monitoring is recommended in this setting.</td>
</tr>
<tr>
<td></td>
<td>ATV/c, ATV/r, LPV/r</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Stones</strong>&lt;br&gt;Nephrolithiasis and cholelithiasis</td>
<td>ATV, ATV/c, ATV/r</td>
<td>DRV/c, DRV/r, INSTI, or NNRTI</td>
<td></td>
<td>Assuming that ATV is believed to be causing the stones.</td>
</tr>
</tbody>
</table>

<sup>a</sup> In patients with chronic active HBV infection, another agent active against HBV should be substituted for TDF.

<sup>b</sup> ABC should be used only in patients known to be HLA-B<sup>5701</sup>-negative.

<sup>c</sup> TDF reduces ATV levels; therefore, unboosted ATV should not be coadministered with TDF. Long-term data for unboosted ATV are unavailable.

**Key to Abbreviations:** ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BMD = bone mineral density; CD4 = CD4 T lymphocyte; CNS = central nervous system; COBI = cobicistat; CrCl = creatine clearance; CV = cardiovascular; d4T = stavudine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; GI = gastrointestinal; HBV = hepatitis B virus; HSR = hypersensitivity reaction; IDV = indinavir; INSTI = integrase strand transfer inhibitor; LDL = low-density lipoprotein; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SCr = serum creatinine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TG = triglycerides; ZDV = zidovudine
### Table 16. Monthly Average Wholesale Price\(^a\) of Commonly Used\(^b\) Antiretroviral Drugs (Last updated October 17, 2017; last reviewed October 17, 2017)

<table>
<thead>
<tr>
<th>ARV Drug (Generic and Brand Names)</th>
<th>Strength, Formulation</th>
<th>Dosing</th>
<th>Tablets, Capsules, or mLs per Month(^c)</th>
<th>AWP(^a) (Monthly)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nucleoside Reverse Transcriptase Inhibitors (NRTIs)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abacavir</td>
<td>300 mg tablet</td>
<td>2 tablets daily</td>
<td>60 tablets</td>
<td>$502.22–$603.33</td>
</tr>
<tr>
<td>• Generic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Ziagen</td>
<td>300 mg tablet</td>
<td>2 tablets daily</td>
<td>60 tablets</td>
<td>$670.37</td>
</tr>
<tr>
<td>• Ziagen</td>
<td>20 mg/mL solution</td>
<td>30 mL daily</td>
<td>900 mL</td>
<td>$660.86</td>
</tr>
<tr>
<td>Emtricitabine</td>
<td>200 mg capsules</td>
<td>1 cap daily</td>
<td>30 capsules</td>
<td>$643.82</td>
</tr>
<tr>
<td>• Emtriva</td>
<td>10 mg/mL solution</td>
<td>24 mL daily</td>
<td>680 mL (28-day supply)</td>
<td>$608.16</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>300 mg tablet</td>
<td>1 tablet daily</td>
<td>30 tablets</td>
<td>$324.33–$429.66</td>
</tr>
<tr>
<td>• Generic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Epivir</td>
<td>300 mg tablet</td>
<td>1 tablet daily</td>
<td>30 tablets</td>
<td>$498.89</td>
</tr>
<tr>
<td>• Epivir</td>
<td>10 mg/mL solution</td>
<td>30 mL daily</td>
<td>900 mL</td>
<td>$498.90</td>
</tr>
<tr>
<td>Tenofovir Disoproxil Fumarate</td>
<td>300 mg tablet</td>
<td>1 tablet daily</td>
<td>30 tablets</td>
<td>$1,279.94</td>
</tr>
<tr>
<td>• Viread</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zidovudine</td>
<td>300 mg tablet</td>
<td>1 tablet twice daily</td>
<td>60 tablets</td>
<td>$54.00–$365.44</td>
</tr>
<tr>
<td>• Generic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>NRTI Combination Products</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abacavir/Lamivudine</td>
<td>600/300 mg tablets</td>
<td>1 tablet daily</td>
<td>30 tablets</td>
<td>$1,395.00</td>
</tr>
<tr>
<td>• Generic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Epzicom</td>
<td>600/300 mg tablets</td>
<td>1 tablet daily</td>
<td>30 tablets</td>
<td>$1,550.05</td>
</tr>
<tr>
<td>Tenofovir Alafenamide/Emtricitabine</td>
<td>25/200 mg tablet</td>
<td>1 tablet daily</td>
<td>30 tablets</td>
<td>$1,881.14</td>
</tr>
<tr>
<td>• Descovy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tenofovir Disoproxil Fumarate/Emtricitabine</td>
<td>300/200 mg tablet</td>
<td>1 tablet daily</td>
<td>30 tablets</td>
<td>$1,881.14</td>
</tr>
<tr>
<td>• Truvada</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zidovudine/Lamivudine</td>
<td>300/150 mg tablet</td>
<td>1 tablet twice daily</td>
<td>60 tablets</td>
<td>$877.85–$931.61</td>
</tr>
<tr>
<td>• Generic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Combivir</td>
<td>300/150 mg tablet</td>
<td>1 tablet twice daily</td>
<td>60 tablets</td>
<td>$1,081.70</td>
</tr>
<tr>
<td>Abacavir Sulfate/Zidovudine/Lamivudine</td>
<td>300/300/150 mg tablet</td>
<td>1 tablet twice daily</td>
<td>60 tablets</td>
<td>$1,738.46</td>
</tr>
<tr>
<td>• Generic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Trizivir</td>
<td>300/300/150 mg tablet</td>
<td>1 tablet twice daily</td>
<td>60 tablets</td>
<td>$1,931.64</td>
</tr>
<tr>
<td>ARV Drug (Generic and Brand Names)</td>
<td>Strength, Formulation</td>
<td>Dosing</td>
<td>Tablets, Capsules, or mLs per Monthc</td>
<td>AWP* (Monthly)</td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>-----------------------</td>
<td>--------</td>
<td>--------------------------------------</td>
<td>----------------</td>
</tr>
<tr>
<td>Efavirenz</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Sustiva</td>
<td>600 mg tablet</td>
<td>1 tablet daily</td>
<td>30 tablets</td>
<td>$1,176.74</td>
</tr>
<tr>
<td>Etravirine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Intelence</td>
<td>200 mg tablet</td>
<td>1 tablet twice daily</td>
<td>60 tablets</td>
<td>$1,411.42</td>
</tr>
<tr>
<td>Nevirapine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Generic</td>
<td>200 mg tablet</td>
<td>1 tablet twice daily</td>
<td>60 tablets</td>
<td>$648.19–$650.70</td>
</tr>
<tr>
<td>• Viramune</td>
<td>200 mg tablet</td>
<td>1 tablet twice daily</td>
<td>60 tablets</td>
<td>$967.63</td>
</tr>
<tr>
<td>• Viramune XR</td>
<td>400 mg tablet</td>
<td>1 tablet daily</td>
<td>30 tablets</td>
<td>$897.46</td>
</tr>
<tr>
<td>Rilpivirine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Edurant</td>
<td>25 mg tablet</td>
<td>1 tablet daily</td>
<td>30 tablets</td>
<td>$1,160.10</td>
</tr>
<tr>
<td><strong>Protease Inhibitors (PIs)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atazanavir</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Reyataz</td>
<td>200 mg capsule</td>
<td>2 capsules daily</td>
<td>60 capsule</td>
<td>$1,755.91</td>
</tr>
<tr>
<td>• Reyataz</td>
<td>300 mg capsuled</td>
<td>1 capsule daily</td>
<td>30 capsule</td>
<td>$1,739.50</td>
</tr>
<tr>
<td>Atazanavir/Cobicistat</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Evolaz</td>
<td>300/150 mg tablet</td>
<td>1 tablet daily</td>
<td>30 tablets</td>
<td>$1,926.56</td>
</tr>
<tr>
<td>Darunavir</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Prezista</td>
<td>600 mg tablet</td>
<td>1 tablet twice daily</td>
<td>60 tablets</td>
<td>$1,757.77</td>
</tr>
<tr>
<td>• Prezista</td>
<td>800 mg tablet</td>
<td>1 tablet daily</td>
<td>30 tablets</td>
<td>$1,757.77</td>
</tr>
<tr>
<td>• Prezista</td>
<td>100 mg/mL suspension²</td>
<td>8 mL daily</td>
<td>240 mL</td>
<td>$1,171.85</td>
</tr>
<tr>
<td>• Prezista</td>
<td></td>
<td>6 mL twice daily</td>
<td>360 mL</td>
<td>$1,757.77</td>
</tr>
<tr>
<td>Darunavir/Cobicistat</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Prezobix</td>
<td>800/150 mg tablet</td>
<td>1 tablet daily</td>
<td>30 tabs</td>
<td>$2,009.23</td>
</tr>
<tr>
<td>Lopinavir/Ritonavir</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Kaletra</td>
<td>200/50 mg tablet</td>
<td>2 capsules twice daily or 4 capsules once daily</td>
<td>120 capsules</td>
<td>$1,160.50</td>
</tr>
<tr>
<td>• Kaletra</td>
<td>80/20 mg per mL solution</td>
<td>5 mL twice daily</td>
<td>300 mL</td>
<td>$1,087.97</td>
</tr>
<tr>
<td>Tipranavir</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Aptivus</td>
<td>250 mg capsulee</td>
<td>2 capsules twice daily</td>
<td>120 capsules</td>
<td>$1,786.73</td>
</tr>
<tr>
<td>Integrase Strand Transfer Inhibitors (INSTIs)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dolutegravir</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Tivicay</td>
<td>50 mg tablet</td>
<td>1 tablet once daily</td>
<td>30 tablets</td>
<td>$1,842.82</td>
</tr>
<tr>
<td>• Tivicay</td>
<td>50 mg tablet</td>
<td>1 tablet twice daily</td>
<td>60 tablets</td>
<td>$3,685.64</td>
</tr>
<tr>
<td>Raltegravir</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Isentress</td>
<td>400 mg tablet</td>
<td>1 tablet twice daily</td>
<td>60 tablets</td>
<td>$1,667.52</td>
</tr>
<tr>
<td>• Isentress HD</td>
<td>600 mg tablet</td>
<td>2 tablets once daily</td>
<td>60 tablets</td>
<td>$1,667.52</td>
</tr>
<tr>
<td>Fusion Inhibitor</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enfuvirtide</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Fuzeon</td>
<td>90 mg injection kit</td>
<td>1 injection twice daily</td>
<td>60 doses (1 kit)</td>
<td>$4,302.67</td>
</tr>
<tr>
<td>CCR5 Antagonist</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maraviroc</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Selzentry</td>
<td>150 mg tablet</td>
<td>1 tablet twice daily</td>
<td>60 tablets</td>
<td>$1,679.68</td>
</tr>
<tr>
<td>• Selzentry</td>
<td>300 mg tablet</td>
<td>1 tablet twice daily</td>
<td>60 tablets</td>
<td>$1,679.68</td>
</tr>
<tr>
<td>• Selzentry</td>
<td>300 mg tablet</td>
<td>2 tablets twice daily</td>
<td>120 tablets</td>
<td>$3,359.36</td>
</tr>
</tbody>
</table>

*Last updated October 17, 2017; last reviewed October 17, 2017*
### Coformulated Combination Products as Single Tablet Regimens

<table>
<thead>
<tr>
<th>ARV Drug (Generic and Brand Names)</th>
<th>Strength, Formulation</th>
<th>Dosing</th>
<th>Tablets, Capsules, or mLs per Month</th>
<th>AWP(^a) (Monthly)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dolutegravir/Abacavir/Lamivudine</td>
<td>50/600/300 mg tablet</td>
<td>1 tablet daily</td>
<td>30 tablets</td>
<td>$3,118.62</td>
</tr>
<tr>
<td>• Triumeq</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Efavirenz/Tenofovir Disoproxil Fumarate/Emtricitabine</td>
<td>600/300/200 mg tablet</td>
<td>1 tablet daily</td>
<td>30 tablets</td>
<td>$3,057.89</td>
</tr>
<tr>
<td>• Atripla</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elvitegravir/Cobicistat/Tenofovir Alafenamide/Emtricitabine</td>
<td>150/150/10/200 mg tablet</td>
<td>1 tablet daily</td>
<td>30 tablets</td>
<td>$3,306.92</td>
</tr>
<tr>
<td>• Genvoya</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elvitegravir/Cobicistat/Tenofovir Disoproxil Fumarate/Emtricitabine</td>
<td>150/150/300/200 mg tablet</td>
<td>1 tablet daily</td>
<td>30 tablets</td>
<td>$3,707.99</td>
</tr>
<tr>
<td>• Stribild</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rilpivirine/Tenofovir Alafenamide/ Emtricitabine</td>
<td>25/25/200 mg tablet</td>
<td>1 tablet daily</td>
<td>30 tablets</td>
<td>$3,009.29</td>
</tr>
<tr>
<td>• Odefsey</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rilpivirine/Tenofovir Disoproxil Fumarate/Emtricitabine</td>
<td>25/300/200 mg tablet</td>
<td>1 tablet daily</td>
<td>30 tablets</td>
<td>$3,216.92</td>
</tr>
<tr>
<td>• Complera</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Pharmacokinetic Enhancers (Boosters)

<table>
<thead>
<tr>
<th>ARV Drug (Generic and Brand Names)</th>
<th>Strength, Formulation</th>
<th>Dosing</th>
<th>Tablets, Capsules, or mLs per Month</th>
<th>AWP(^a) (Monthly)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cobicistat</td>
<td>150 mg tablet</td>
<td>1 tablet daily</td>
<td>30 tablets</td>
<td>$246.84</td>
</tr>
<tr>
<td>• Tybost</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ritonavir: Total daily dose depends on the dose of the concomitant PI (100 mg once or twice daily, or 200 mg twice daily)</td>
<td>100 mg tablet</td>
<td>1 tablet once daily</td>
<td>30 tablets</td>
<td>$308.60</td>
</tr>
<tr>
<td>• Norvir</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Norvir</td>
<td>80 mg/mL solution</td>
<td>100 mg daily</td>
<td>37.5 mL (of a 240 mL bottle)</td>
<td>$270.04</td>
</tr>
</tbody>
</table>

\(^a\) AWP = average wholesale price. Note that the AWP may not represent the pharmacy acquisition price or the price paid by public and private payors or consumers. Source: http://www.micromedexsolutions.com. Accessed September 2017.

\(^b\) The following less commonly used ARV drugs are not included in this table: delavirdine, didanosine, fosamprenavir, indinavir, nelfinavir, saquinavir, and stavudine.

\(^c\) Represents 30 days or as specified.

\(^d\) Should be used in combination with ritonavir or cobicistat. Please refer to Appendix B, Table 3 for ritonavir doses.

\(^e\) Should be used in combination with ritonavir. Please refer to Appendix B, Table 3 for ritonavir doses.

**Key to Acronyms:** ARV = antiretroviral; XR = extended release
Table 17. Mechanisms of Antiretroviral-Associated Drug Interactions  (page 1 of 2)

PK interactions may occur during absorption, metabolism, or elimination of the ARV and/or the interacting drugs. This table does not include a comprehensive list of all possible mechanisms of interactions for individual ARV drugs (e.g., transporters); however, the table lists the most common mechanisms of known interactions and focuses on absorption and CYP- and UGT1A1-mediated interactions.

Note: Ellipses [...] indicates that there are no clinically relevant interactions by these mechanisms.

<table>
<thead>
<tr>
<th>ARV Drugs by Drug Class</th>
<th>Mechanisms That May Affect Oral Absorption of ARV Drugs</th>
<th>Enzymes That Metabolize or are Induced or Inhibited by ARV Drugs</th>
<th>Other Mechanisms of Known Drug Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Increasing Gastric pH</td>
<td>Cationic Chelation</td>
<td>P-glycoprotein</td>
</tr>
<tr>
<td>INSTIs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DTG</td>
<td>...</td>
<td>Concentration decreased by products containing polyvalent cations (e.g., Ca, Mg, Al, Fe, Zn)</td>
<td>Substrate</td>
</tr>
<tr>
<td>EVG</td>
<td>...</td>
<td>...</td>
<td>3A4</td>
</tr>
<tr>
<td>RAL</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>PK Enhancers (Boosters)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>COBI</td>
<td>...</td>
<td>...</td>
<td>Inhibitor</td>
</tr>
<tr>
<td>RTV</td>
<td>...</td>
<td>...</td>
<td>Substrate, inhibitor</td>
</tr>
<tr>
<td>PIs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATV</td>
<td>Concentration decreased</td>
<td>...</td>
<td>Substrate, inducer, inhibitor</td>
</tr>
</tbody>
</table>

Note: When PIs are coadministered with PK enhancers (boosters), the pharmacologic properties of both agents should be considered when assessing potential drug interactions.
### Table 17. Mechanisms of Antiretroviral-Associated Drug Interactions (page 2 of 2)

<table>
<thead>
<tr>
<th>ARV Drugs by Drug Class</th>
<th>Mechanisms That May Affect Oral Absorption of ARV Drugs</th>
<th>Enzymes That Metabolize or are Induced or Inhibited by ARV Drugs</th>
<th>Other Mechanisms of Known Drug Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Increasing Gastric pH</td>
<td>Cationic Chelation</td>
<td>P-glycoprotein</td>
</tr>
<tr>
<td><strong>PIs, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DRV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FPV</td>
<td>Concentration decreased by H2 antagonist</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td>LPV</td>
<td>...</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td>SQV</td>
<td>...</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td>TPV</td>
<td>...</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td><strong>NNRTIs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EFV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ETR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NVP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RPV</td>
<td>Concentration decreased</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td><strong>NRTIs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FTC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3TC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TAF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TDF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ZDV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CCR5 Antagonist</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MVC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fusion Inhibitor</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T20</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Key to Acronyms:** 3TC = lamivudine; ABC = abacavir; Al = aluminum; ARV = antiretroviral; ATV = atazanavir; Ca = calcium; COBI = cobicistat; CYP = cytochrome P; DRV = darunavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; Fe = iron; FPV = fosamprenavir; FTC = emtricitabine; INSTI = integrase strand transfer inhibitor; LPV = lopinavir; MATE = multidrug and toxin extrusion transporter; Mg = magnesium; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitors; NRTI = nucleoside reverse transcriptase inhibitors; NVP = nevirapine; OCT2 = organic cation transporter 2; OATP = organic anion-transporting polypeptide; PK = pharmacokinetic; PI = protease inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQV = saquinavir; T20 = enfuvirtide; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV = tipranavir; UGT = uridine diphosphate glucuronosyltransferase; ZDV = zidovudine; Zn = zinc
This table provides known or predicted information regarding PK interactions between PIs and non-ARV drugs. When information is available, interactions for specific PK-boosted (with either RTV or COBI) and unboosted ATV are listed separately. The term “All PIs” refers to both unboosted ATV and PIs boosted with either RTV or COBI, except the PIs noted below. For interactions between ARV agents and for dosing recommendations, refer to Tables 18c, 19a, and 19b.

Recommendations for managing a particular drug interaction may differ depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or if a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly.

Note: Fosamprenavir (FPV), indinavir (IDV), nelfinavir (NFV), and saquinavir (SQV) are not included in this table. Please refer to the Food and Drug Administration product labels for FPV, IDV, NFV, and SQV for information regarding drug interactions with these PIs.

### Table 18a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 1 of 17)

<table>
<thead>
<tr>
<th>Concomitant Drug</th>
<th>PI</th>
<th>Effect on PI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acid Reducers</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antacids</td>
<td>ATV, ATV/c, ATV/r</td>
<td>When given simultaneously, ↓ ATV expected</td>
<td>Give ATV at least 2 hours before or 1 to 2 hours after antacids or buffered medications.</td>
</tr>
<tr>
<td></td>
<td>TPV/r</td>
<td>TPV AUC ↓ 27%</td>
<td>Give TPV at least 2 hours before or 1 hour after antacids.</td>
</tr>
<tr>
<td><strong>H2 Receptor Antagonists</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATV (unboosted)</td>
<td>↓ ATV</td>
<td></td>
<td>Give ATV at least 2 hours before and at least 10 hours after the H2 receptor antagonist.</td>
</tr>
<tr>
<td>ATV/c, ATV/r</td>
<td>↓ ATV</td>
<td></td>
<td>H2 receptor antagonist single dose should not exceed a dose equivalent to famotidine 20 mg, and the total daily dose should not exceed a dose equivalent to famotidine 20 mg BID in PI-naive patients. Unboosted ATV + famotidine should not be used in combination in PI-experienced patients.</td>
</tr>
<tr>
<td>DRV/c, DRV/r, LPV/r</td>
<td>↔ demonstrated or expected</td>
<td>No dose adjustment necessary.</td>
<td></td>
</tr>
<tr>
<td><strong>PPIs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATV (unboosted)</td>
<td>↓ ATV</td>
<td>PPIs are not recommended in patients receiving unboosted ATV. In these patients, consider alternative acid-reducing agents, RTV or COBI boosting, or alternative PIs.</td>
<td></td>
</tr>
<tr>
<td>ATV/c, ATV/r</td>
<td>↓ ATV</td>
<td>PPIs should not exceed a dose equivalent to omeprazole 20 mg daily in PI-naive patients. PPIs should be administered at least 12 hours before ATV/c or ATV/r.</td>
<td>PPIs are not recommended in PI-experienced patients.</td>
</tr>
<tr>
<td>DRV/c, LPV/r</td>
<td>↔ expected</td>
<td>No dose adjustment necessary.</td>
<td></td>
</tr>
<tr>
<td>DRV/r</td>
<td>Omeprazole AUC ↓ 42%</td>
<td>No dose adjustment necessary. If there is a lack of symptomatic relief; increase omeprazole dose to no more than 40 mg daily if needed.</td>
<td></td>
</tr>
</tbody>
</table>
### Concomitant Drug Effects on PI and/or Concomitant Drug Concentrations

#### Acid Reducers, continued

<table>
<thead>
<tr>
<th>Concomitant Drug</th>
<th>PI</th>
<th>Effect on PI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PPIs, continued</strong></td>
<td>TPV/r</td>
<td>Omeprazole AUC ↓ 70%</td>
<td>Coadministration is not recommended. If coadministration is necessary, dose increases of omeprazole may be considered based on clinical response.</td>
</tr>
</tbody>
</table>

#### Anticoagulants and Antiplatelets

<table>
<thead>
<tr>
<th>Concomitant Drug</th>
<th>PI</th>
<th>Effect on PI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Apixaban</strong></td>
<td>PI/c, PI/r</td>
<td>↑ apixaban expected</td>
<td>Coadministration is not recommended. Consider alternative ARV or warfarin. If coadministration is necessary, reduce apixaban dose by 50% and monitor for apixaban toxicity.</td>
</tr>
<tr>
<td><strong>Betrixaban</strong></td>
<td>PI/r</td>
<td>↑ or ↓ betrixaban possible</td>
<td>Coadministration is not recommended. Consider alternative ARV or warfarin.</td>
</tr>
<tr>
<td></td>
<td>ATV/c, DRV/c</td>
<td>↑ betrixaban expected</td>
<td>Coadministration is not recommended. Consider alternative ARV or warfarin.</td>
</tr>
<tr>
<td><strong>Dabigatran</strong></td>
<td>PI/r</td>
<td>With RTV 100 mg + dabigatran taken simultaneously: ↔ dabigatran</td>
<td>The extent of interaction of PI/r + dabigatran is unknown. Consider alternative ARV or warfarin.</td>
</tr>
<tr>
<td></td>
<td>ATV/c, DRV/c</td>
<td>With COBI 150 mg: dabigatran AUC ↓ 29%</td>
<td>Coadministration is not recommended. Consider alternative ARV or warfarin.</td>
</tr>
<tr>
<td><strong>Edoxaban</strong></td>
<td>PI/r</td>
<td>↑ or ↓ edoxaban possible</td>
<td>Coadministration is not recommended. Consider alternative ARV or warfarin.</td>
</tr>
<tr>
<td></td>
<td>ATV/c, DRV/c</td>
<td>↑ edoxaban expected</td>
<td>Coadministration is not recommended. Consider alternative ARV or warfarin.</td>
</tr>
<tr>
<td><strong>Rivaroxaban</strong></td>
<td>PI/c, PI/r</td>
<td>↑ rivaroxaban expected</td>
<td>Coadministration is not recommended. Consider alternative ARV or warfarin.</td>
</tr>
<tr>
<td><strong>Ticagrelor</strong></td>
<td>All PIs</td>
<td>↑ ticagrelor expected</td>
<td>Coadministration is not recommended. Consider alternative ARV or warfarin.</td>
</tr>
<tr>
<td><strong>Vorapaxar</strong></td>
<td>All PIs</td>
<td>↑ vorapaxan expected</td>
<td>Coadministration is not recommended. Consider alternative ARV or warfarin.</td>
</tr>
<tr>
<td><strong>Warfarin</strong></td>
<td>PI/r</td>
<td>↓ warfarin possible</td>
<td>Monitor INR closely when stopping or starting PI/r and adjust warfarin dose accordingly.</td>
</tr>
<tr>
<td></td>
<td>ATV/c, DRV/c</td>
<td>No data</td>
<td>Monitor INR closely when stopping or starting PI/c and adjust warfarin dose accordingly. If switching between RTV and COBI, the effect of COBI on warfarin is not expected to be equivalent to RTV’s effect on warfarin.</td>
</tr>
</tbody>
</table>

#### Anticonvulsants

<table>
<thead>
<tr>
<th>Concomitant Drug</th>
<th>PI</th>
<th>Effect on PI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Carbamazepine</strong></td>
<td>ATV (unboosted)</td>
<td>May ↓ PI levels substantially</td>
<td><strong>Do not coadminister.</strong> Consider alternative anticonvulsant or ARV.</td>
</tr>
<tr>
<td></td>
<td>ATV/c, DRV/c</td>
<td>↓ cobicistat expected</td>
<td><strong>Contraindicated.</strong></td>
</tr>
<tr>
<td></td>
<td>ATV/r, LPV/r, TPV/r</td>
<td>↑ carbamazepine possible</td>
<td>Consider alternative anticonvulsant or monitor levels of both drugs and assess virologic response. <strong>Do not coadminister with LPV/r once daily.</strong></td>
</tr>
</tbody>
</table>

---

Table 18a. Drug Interactions Between Protease Inhibitors and Other Drugs  *(Last updated October 17, 2017; last reviewed October 17, 2017)*  (page 2 of 17)
### Concomitant Drug

<table>
<thead>
<tr>
<th>Concomitant Drug</th>
<th>PI</th>
<th>Effect on PI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anticonvulsants, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbamazepine, continued</td>
<td>DRV/r</td>
<td>Carbamazepine AUC ↑ 45%</td>
<td>Monitor anticonvulsant level and adjust dose accordingly.</td>
</tr>
<tr>
<td>Oxicarbazepine, Eslicarbazepine</td>
<td>All PIs</td>
<td>↓ PI possible</td>
<td>Consider alternative anticonvulsant or ARV. If coadministration is necessary, monitor for virologic response. Consider monitoring anticonvulsant and PI concentration.</td>
</tr>
<tr>
<td>Ethosuximide</td>
<td>All PIs</td>
<td>↑ ethosuximide possible</td>
<td>Clinically monitor for ethosuxamide toxicities.</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>ATV (unboosted)</td>
<td>Lamotrigine: no effect</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td>ATV/r</td>
<td>Lamotrigine AUC ↓ 32%</td>
<td>A dose increase of lamotrigine may be needed; consider monitoring lamotrigine concentration or consider alternative anticonvulsant.</td>
</tr>
<tr>
<td></td>
<td>LPV/r</td>
<td>Lamotrigine AUC ↓ 50%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>DRV/r, TPV/r</td>
<td>↓ lamotrigine possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ATV/c, DRV/c</td>
<td>No data</td>
<td>Monitor lamotrigine concentration or consider alternative anticonvulsant.</td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>ATV/c, DRV/c</td>
<td>↓ cobicistat expected</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ PI levels expected</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ATV (unboosted), PI/r</td>
<td>May ↓ PI levels substantially</td>
<td>Consider alternative anticonvulsant or monitor levels of both drugs and assess virologic response.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Do not coadminister with LPV/r once daily or unboosted ATV.</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>ATV (unboosted)</td>
<td>May ↓ PI levels substantially</td>
<td>Do not coadminister. Consider alternative anticonvulsant or ATV/r.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ATV/r, DRV/r, TPV/r</td>
<td>↓ phenytoin possible</td>
<td>Consider alternative anticonvulsant or monitor levels of both drugs and assess virologic response.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ PI possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ATV/c, DRV/c</td>
<td>↓ cobicistat expected</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ PI levels expected</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LPV/r</td>
<td>Phenytoin AUC ↓ 31%</td>
<td>Consider alternative anticonvulsant or monitor levels of both drugs and assess virologic response.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LPV/r AUC ↓ 33%</td>
<td>Do not coadminister with LPV/r once daily.</td>
</tr>
<tr>
<td>Valproic Acid</td>
<td>PI/c, PI/r</td>
<td>↓ or ↔ VPA possible</td>
<td>Monitor VPA levels and virologic response. Monitor for LPV-related toxicities.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LPV AUC ↑ 75%</td>
<td></td>
</tr>
</tbody>
</table>

### Antidepressants, Anxiolytics, and Antipsychotics (also see Sedative/Hypnotics section below)

<table>
<thead>
<tr>
<th>Drug</th>
<th>PI</th>
<th>Effect on PI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bupropion</td>
<td>LPV/r</td>
<td>Bupropion AUC ↓ 57%</td>
<td>Titrate bupropion dose based on clinical response.</td>
</tr>
<tr>
<td></td>
<td>TPV/r</td>
<td>Bupropion AUC ↓ 46%</td>
<td></td>
</tr>
<tr>
<td>Buspirone</td>
<td>All PIs</td>
<td>↑ buspirone expected</td>
<td>Use a low dose of buspirone with caution and titrate buspirone dose based on clinical response.</td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>All PIs</td>
<td>↑ or ↓ PI possible</td>
<td>Consider alternative therapeutic agent.</td>
</tr>
<tr>
<td>Lurasidone</td>
<td>PI/c, PI/r</td>
<td>↑ lurasidone expected</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td></td>
<td>ATV (unboosted)</td>
<td>↑ lurasidone expected</td>
<td>Consider alternative therapy. If coadministration is necessary, reduce lurasidone dose by 50%.</td>
</tr>
</tbody>
</table>
### Antidepressants, Anxiolytics, and Antipsychotics (also see Sedative/Hypnotics section below), continued

<table>
<thead>
<tr>
<th>Concomitant Drug</th>
<th>PI</th>
<th>Effect on PI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Other Selective Serotonin Reuptake Inhibitors (SSRIs)</strong> (e.g., citalopram, escitalopram, fluoxetine, paroxetine, sertraline)</td>
<td>RTV</td>
<td>Escitalopram ↔</td>
<td>Titrate SSRI dose based on clinical response.</td>
</tr>
<tr>
<td></td>
<td>DRV/r</td>
<td>Escitalopram ↔</td>
<td>Paroxetine AUC ↓ 39%</td>
</tr>
<tr>
<td></td>
<td>ATV/r, LPV/r, TPV/r</td>
<td>Sertraline AUC ↓ 49%</td>
<td>No data</td>
</tr>
<tr>
<td></td>
<td>ATV/c, DRV/c</td>
<td>Effects unknown</td>
<td>Titrate SSRI dose using the lowest available initial or maintenance dose.</td>
</tr>
</tbody>
</table>

| Pimozide | All PIs | ↑ pimozide expected | Contraindicated. |

| Quetiapine | All PIs | ↑ quetiapine expected | Starting Quetiapine in a Patient Receiving a PI: Start quetiapine at the lowest dose and titrate up as needed. Monitor for quetiapine effectiveness and adverse effects. |
| | | | Starting a PI in a Patient Receiving a Stable Dose of Quetiapine: Reduce quetiapine dose to 1/6 of the original dose. Closely monitor for quetiapine effectiveness and adverse effects. |

| Other Antipsychotics (e.g., perphenazine, risperidone, thioridazine) | PI/c, PI/r | ↑ antipsychotic possible | Titrate antipsychotic dose using the lowest initial dose, or adjust maintenance dose accordingly. Monitor for toxicities. |

| Trazodone | All PIs | RTV 200 mg BID (for 2 days) ↑ trazodone AUC 240% | Use lowest dose of trazodone and monitor for CNS and CV adverse effects. |

| Tricyclic Antidepressants | All PIs | ↑ TCA expected | Use lowest possible TCA dose and titrate based on clinical assessment and/or drug levels. |

### Antifungals

| Fluconazole | PI/c, ATV/r, DRV/r, LPV/r | No significant effect observed or expected | No dose adjustment necessary. |
| | TPV/r | TPV AUC ↑ 50% | Fluconazole >200 mg daily is not recommended. If high-dose fluconazole is indicated, consider alternative ARV. |
| Isavuconazole | LPV/r | Isavuconazole AUC ↑ 96% | If coadministered, consider monitoring isavuconazole concentrations and toxicities and assessing virologic response. |
| | | LPV AUC ↓ 27% | |
| | | RTV AUC ↓ 31% | |

| Itraconazole | All PIs except LPV/r | ↑ itraconazole possible |
| | | ↑ or ↓ PI possible |

| Itraconazole | All PIs | ↑ itraconazole possible |
| | | ↑ PI possible |

| Itraconazole | All PIs | ↑ itraconazole possible |
| | | ↑ PI possible |

Consider monitoring itraconazole level to guide dosage adjustments. Doses >200 mg/day are not recommended with PI/r, ATV/c, or DRV/c unless dosing is guided by itraconazole levels.
Table 18a. Drug Interactions Between Protease Inhibitors and Other Drugs  (Last updated October 17, 2017; last reviewed October 17, 2017) (page 5 of 17)

<table>
<thead>
<tr>
<th>Concomitant Drug</th>
<th>PI</th>
<th>Effect on PI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antifungals, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| **Posaconazole** | ATV/r | ATV AUC ↑ 146%  
↑ posaconazole possible | If coadministered, monitor for PI adverse effects. Consider monitoring posaconazole concentrations and toxicities. |
| | ATV | ATV AUC ↑ 268%  
↑ posaconazole possible | |
| | ATV/c, DRV/c, DRV/r, LPV/r, TPV/r | ↑ PI possible  
↑ posaconazole possible | |
| **Voriconazole** | ATV (unboosted) | ↑ voriconazole possible  
↑ PI possible | Monitor for toxicities. |
| | All PI/r | RTV 400 mg BID ↓ voriconazole AUC 82%  
RTV 100 mg BID ↓ voriconazole AUC 39% | Do not coadminister voriconazole and RTV or COBI unless benefit outweighs risk. If coadministered, consider monitoring voriconazole concentration and adjust dose accordingly. |
| | ATV/c, DRV/c | Effects unknown | |
| **Antihyperglycemics** | | | |
| **Canagliflozin** | PI/r | ↓ canagliflozin expected | If a patient is already tolerating canagliflozin 100 mg daily, has an eGFR >60 mL/min/1.73m², and requires additional glycemic control, consider increasing canagliflozin dose to 300 mg daily.  
If used in combination, monitor glycemic control. |
| | PI/c | ↓ canagliflozin possible | |
| **Saxagliptin** | All PIs | ↑ saxagliptin expected | Limit saxagliptin dose to 2.5 mg once daily. |
| **Dapagliflozin/ Saxagliptin** | All PIs | ↑ saxagliptin expected | Do not coadminister, as this coformulated drug contains 5 mg of saxagliptin. |
| **Antimalarials** | | | |
| **Artemether/ Lumefantrine** | DRV/r | Artemether AUC ↓ 16%  
DHA+ AUC ↓ 18%  
Lumefantrine AUC ↑ 2.5-fold | Clinical significance unknown. If used, monitor closely for antimalarial efficacy and lumefantrine toxicity. |
| | DRV/c | ↑ lumefantrine expected  
Effect on artemether unknown | |
| | LPV/r | Artemether AUC ↓ 40%  
DHA AUC ↓ 17%  
Lumefantrine AUC ↑ 470% | |
| **Artesunate/ Mefloquine** | LPV/r | Dihydroartemisinin AUC ↓ 49%  
Mefloquine AUC ↓ 28%  
LPV ↔ | Clinical significance unknown. If used, monitor closely for antimalarial efficacy. |
### Table 18a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 6 of 17)

<table>
<thead>
<tr>
<th>Concomitant Drug</th>
<th>PI</th>
<th>Effect on PI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antimalarials, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Atovaquone/Proguanil | ATV/r, LPV/r | With ATV/r:  
- ↓ atovaquone AUC 46%  
- ↓ proguanil AUC 41%  
With LPV/r:  
- ↓ atovaquone AUC 74%  
- ↓ proguanil AUC 38% | No dose recommendation. Consider alternative drug for malaria prophylaxis, if possible. |
| Mefloquine | RTV | With RTV 200 mg BID:  
- RTV AUC ↓ 31%, Cmin ↓ 43%  
- ↔ mefloquine | Use with caution. Effect on exposure of RTV-boosted PIs is unknown. |
| **Antimycobacterials (for treatment of Mycobacterium tuberculosis and nontuberculosis mycobacterial infections)** |
| Bedaquiline | All PIs | With LPV/r:  
- Bedaquiline AUC ↑ 1.9-fold  
With other PI/r, ATV/c, or DRV/c:  
- ↑ bedaquiline possible | Clinical significance unknown. Use with caution if benefit outweighs the risk and monitor for QTc prolongation and liver function tests. |
| Clarithromycin | ATV (unboosted) | Clarithromycin AUC ↑ 94% | May cause QTc prolongation. Reduce clarithromycin dose by 50%. Consider alternative therapy (e.g., azithromycin). |
| | All PIs | ↑ clarithromycin expected  
DRV/r ↑ clarithromycin AUC 57%  
LPV/r ↑ clarithromycin expected  
RTV 500 mg BID ↑ clarithromycin 77%  
TPV/r ↑ clarithromycin 19%  
Clarithromycin ↑ TPV 66% | Consider alternative macrolide (e.g., azithromycin).  
Monitor for clarithromycin-related toxicities or consider an alternative macrolide (e.g., azithromycin).  
Reduce clarithromycin dose by 50% in patients with CrCl 30–60 mL/min.  
Reduce clarithromycin dose by 75% in patients with CrCl <30 mL/min. |
| Rifabutin | ATV (unboosted) | ↑ rifabutin AUC expected | Rifabutin 150 mg daily or 300 mg three times a week. |
| | ATV/r | Compared with rifabutin (300 mg once daily) alone, rifabutin (150 mg once daily) + ATV/r:  
- rifabutin AUC ↑ 110% and metabolite AUC ↑ 2101% | Rifabutin 150 mg once daily or 300 mg three times a week.  
Monitor for antimycobacterial activity and consider therapeutic drug monitoring.  
PK data reported in this table are results from healthy volunteer studies. Lower rifabutin exposure has been reported in patients with HIV than in the healthy study participants. |
| | DRV/r | Compared with rifabutin (300 mg once daily) alone, rifabutin (150 mg every other day) + DRV/r:  
- rifabutin AUC ↔ and metabolite AUC ↑ 881% | |
| | LPV/r | Compared with rifabutin (300 mg daily) alone, rifabutin (150 mg once daily) + LPV/r:  
- rifabutin and metabolite AUC ↑ 473% | |
Table 18a. Drug Interactions Between Protease Inhibitors and Other Drugs  
(Last updated October 17, 2017; last reviewed October 17, 2017)  
(page 7 of 17)

<table>
<thead>
<tr>
<th>Concomitant Drug</th>
<th>PI</th>
<th>Effect on PI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antimycobacterials (for treatment of <em>Mycobacterium tuberculosis</em> and nontuberculosis mycobacterial infections), continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rifabutin, continued</td>
<td>TPV/r</td>
<td>Rifabutin and metabolite AUC ↑ 333%</td>
<td></td>
</tr>
<tr>
<td>Rifampin</td>
<td>All PIs</td>
<td>↓ PI concentration by &gt;75%</td>
<td><strong>Contraindicated.</strong> Additional RTV does not overcome this interaction and may increase hepatotoxicity. Additional COBI is not recommended. Consider rifabutin if a rifamycin is indicated.</td>
</tr>
<tr>
<td>Rifapentine</td>
<td>All PIs</td>
<td>↓ PI expected</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
<tr>
<td><strong>Antipneumocystis and Antitoxoplasmosis Drug</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atovaquone</td>
<td>ATV/r</td>
<td>Atovaquone ↔</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td><strong>Cardiac Medications</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amiodarone</td>
<td>TPV/r</td>
<td>↑ both amiodarone and PI possible</td>
<td><strong>Contraindicated.</strong></td>
</tr>
<tr>
<td>All PIs except TPV/r</td>
<td>↑ both amiodarone and PI possible</td>
<td>Use with caution. Monitor for amiodarone toxicity and consider ECG and amiodarone drug level monitoring.</td>
<td></td>
</tr>
<tr>
<td>Antiarrhythmics (e.g., disopyramide, dofetilide, lidocaine, mexiletine, propafenone)</td>
<td>ATV (unboosted)</td>
<td>↑ antiarrhythmic possible</td>
<td>Consider alternative antiarrhythmics or ARV. If coadministered, monitor for antiarrhythmic toxicities.</td>
</tr>
<tr>
<td>PI/c, PI/r</td>
<td>↑ antiarrhythmic possible</td>
<td><strong>Do not coadminister.</strong> Consider alternative antiarrhythmics or ARV.</td>
<td></td>
</tr>
<tr>
<td>Dronedarone</td>
<td>ATV (unboosted)</td>
<td>↑ dronedarone possible</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
<tr>
<td>PI/c, PI/r</td>
<td>↑ dronedarone expected</td>
<td><strong>Contraindicated.</strong></td>
<td></td>
</tr>
<tr>
<td>Flecanide</td>
<td>All PIs except TPV/r</td>
<td>↑ flecainide possible</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
<tr>
<td>TPV/r</td>
<td>↑ flecainide expected</td>
<td><strong>Contraindicated.</strong></td>
<td></td>
</tr>
<tr>
<td>Propafenone</td>
<td>All PIs except TPV/r</td>
<td>↑ propafenone possible</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
<tr>
<td>TPV/r</td>
<td>↑ propafenone expected</td>
<td><strong>Contraindicated.</strong></td>
<td></td>
</tr>
<tr>
<td>Quinidine</td>
<td>All PIs except TPV/r</td>
<td>↑ quinidine possible</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
<tr>
<td>TPV/r</td>
<td>↑ quinidine expected</td>
<td><strong>Contraindicated.</strong></td>
<td></td>
</tr>
<tr>
<td>Beta-Blockers (e.g., carvedilol, metoprolol, timolol)</td>
<td>All PIs</td>
<td>↑ beta-blockers possible</td>
<td>May need to decrease beta-blocker dose; adjust dose based on clinical response. Consider using beta-blockers that are not metabolized by CYP450 enzymes (e.g., atenolol, labetalol, nadolol, sotalol).</td>
</tr>
</tbody>
</table>
### Table 18a. Drug Interactions Between Protease Inhibitors and Other Drugs  
**Last updated October 17, 2017; last reviewed October 17, 2017**

<table>
<thead>
<tr>
<th>Concomitant Drug</th>
<th>PI</th>
<th>Effect on PI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiac Medications, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| **Bosentan** | All PIs | LPV/r ↑ bosentan 48-fold (day 4) and 5-fold (day 10) ↓ ATV expected | Do not coadminister bosentan and unboosted ATV.  
In Patients on a PI (Other than Unboosted ATV) >10 Days:  
• Start bosentan at 62.5 mg once daily or every other day.  
In Patients on Bosentan who Require a PI (Other than Unboosted ATV):  
• Stop bosentan ≥36 hours before PI initiation and restart bosentan 10 days after PI initiation at 62.5 mg once daily or every other day.  
When Switching Between COBI and RTV:  
• Maintain same bosentan dose. |
| **Calcium Channel Blockers (CCBs), Except Diltiazem** | All PIs | ↑ dihydropyridine possible  
↑ verapamil possible | Use with caution. Titrate CCB dose and monitor closely. ECG monitoring is recommended when CCB is used with ATV. |
| **Digoxin** | PI/r, PI/c | RTV (200 mg BID) ↑ digoxin AUC 29% and ↑ half-life 43%  
DRV/r ↑ digoxin AUC 36%  
COBI ↑ digoxin C<sub>max</sub> 41%, AUC ↔ | Use with caution. Monitor digoxin levels. Digoxin dose may need to be decreased. Titrate initial digoxin dose. |
| **Diltiazem** | ATV/c, ATVR, ATV (unboosted) | Unboosted ATV ↑ diltiazem AUC 125%  
Greater ↑ likely with ATV/c or ATVR | Decrease diltiazem dose by 50%. ECG monitoring is recommended. |
| | DRV/c, DRV/r, LPV/r, TPV/r | ↑ diltiazem possible | Use with caution. Adjust diltiazem according to clinical response and toxicities. |
| **Eplerenone** | PI/c, PI/r | ↑ eplerenone expected | Contraindicated. |
| **Ranolazine** | ATV (unboosted) | ↑ ranolazine possible | Do not coadminister.  
Contraindicated. |
| | PI/c, PI/r | ↑ ranolazine expected | Contraindicated. |
| **Ivabradine** | All PIs | ↑ ivabradine expected | Contraindicated. |
| **Corticosteroids** | | | |
| **Beclomethasone** | DRV/r | 17-BMP (active metabolite) AUC ↔  
RTV 100 mg BID ↑ 17-BMP AUC 2-fold | No dose adjustment necessary. |
| **All PIs except DRV/r** | ↔ expected | No dose adjustment necessary. |
| **Budesonide, Ciclesonide, Fluticasone, Mometasone** | All PIs | ↑ glucocorticoids possible  
RTV 100 mg BID ↑ fluticasone AUC 350-fold | Coadministration can result in adrenal insufficiency and Cushing’s syndrome. Do not coadminister unless potential benefits of inhaled or intranasal corticosteroid outweigh the risks of systemic corticosteroid adverse effects. Consider an alternative corticosteroid (e.g., beclomethasone). |
### Table 18a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 9 of 17)

<table>
<thead>
<tr>
<th>Concomitant Drug</th>
<th>PI</th>
<th>Effect on PI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Corticosteroids, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Betamethasone, Budesonide Systemic</td>
<td>All PIs</td>
<td>↑ glucocorticoids possible, ↓ PI possible</td>
<td>Coadministration can result in adrenal insufficiency and Cushing’s syndrome. <strong>Do not coadminister unless potential benefits of systemic corticosteroid outweigh the risks of systemic corticosteroid adverse effects.</strong></td>
</tr>
<tr>
<td>Dexamethasone Systemic</td>
<td>All PIs</td>
<td>↑ glucocorticoids possible</td>
<td>Consider alternative corticosteroid for long-term use. If coadministration is necessary, monitor virologic response to ART.</td>
</tr>
<tr>
<td>Prednisone, Prednisolone Systemic</td>
<td>LPV/r</td>
<td>↑ prednisolone AUC 31%</td>
<td>Coadministration may be considered if the potential benefits outweigh the risks of systemic corticosteroid adverse effects. If coadministered, monitor for adrenal insufficiency, Cushing’s syndrome, and other corticosteroid-associated toxicities.</td>
</tr>
<tr>
<td></td>
<td>All PIs</td>
<td>↑ prednisolone possible</td>
<td></td>
</tr>
<tr>
<td>Betamethasone, Methylprednisolone, Triamcinolone Local injections, including intra-articular, epidural, or intra-orbital</td>
<td>All PIs</td>
<td>↑ glucocorticoids expected</td>
<td><strong>Do not coadminister.</strong> Coadministration can result in adrenal insufficiency and Cushing’s syndrome.</td>
</tr>
</tbody>
</table>

### Hepatitis C Direct-Acting Antiviral Agents

<table>
<thead>
<tr>
<th></th>
<th>PI</th>
<th>Effect on PI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daclatasvir</td>
<td>ATV/c, ATV/r</td>
<td>↑ daclatasvir</td>
<td>Decrease daclatasvir dose to 30 mg once daily.</td>
</tr>
<tr>
<td></td>
<td>ATV (unboosted), DRV/c, DRV/r, LPV/r</td>
<td>↔ daclatasvir</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td>TPV/r</td>
<td>No data</td>
<td>No dosing recommendations available at this time.</td>
</tr>
<tr>
<td>Dasabuvir + Paritaprevir/Ombitasvir/RTV</td>
<td>ATV (unboosted)</td>
<td>ATV ↔</td>
<td>ATV 300 mg alone, <strong>without COBI or additional RTV,</strong> should be given in the morning with dasabuvir + paritaprevir/ombitasvir/RTV.</td>
</tr>
<tr>
<td></td>
<td>DRV</td>
<td>DRV C&lt;sub&gt;min&lt;/sub&gt; ↓ 43% to 48%</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
<tr>
<td></td>
<td>LPV/r</td>
<td>Paritaprevir AUC ↑ 117%</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
<tr>
<td></td>
<td>ATV/c, DRV/c, TPV/r</td>
<td>No data</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
</tbody>
</table>
### Hepatitis C Direct-Acting Antiviral Agents, continued

<table>
<thead>
<tr>
<th>Concomitant Drug</th>
<th>PI</th>
<th>Effect on PI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
</table>
| **Elbasvir/ Grazoprevir** | ATV/r | Elbasvir AUC ↑ 4.8-fold  
Grazoprevir AUC ↑ 10.6-fold  
ATV ↔ by elbasvir  
ATV AUC ↑ 43% by grazoprevir | Contraindicated.  
May increase the risk of ALT elevations due to a significant increase in grazoprevir plasma concentrations caused by OATP1B1/3 inhibition. |
| | DRV/r | Elbasvir AUC ↑ 66%  
Grazoprevir AUC ↑ 7.5-fold  
DRV ↔ | | |
| | LPV/r | Elbasvir AUC ↑ 3.7-fold  
Grazoprevir AUC ↑ 12.9-fold  
LPV ↔ | | |
| | ATV (unboosted), ATV/c, DRV/c, TPV/r | ↑ grazoprevir expected | | |
| **Glecaprevir/ Pibrentasvir** | ATV (unboosted), ATV/c, ATV/r | When Given with ATV/r 300/100 mg Once Daily:  
• Glecaprevir AUC ↑ 6.5-fold  
• Pibrentasvir AUC ↑ 64% | Contraindicated.  
Do not coadminister. |
| | DRV/c, DRV/r | When Given with DRV/r 800/100 mg Once Daily:  
• Glecaprevir AUC ↑ 5-fold  
• ↔ pibrentasvir | Do not coadminister.  
Do not coadminister. |
| | LPV/r | ↑ glecaprevir AUC 4-fold  
↑ pibrentasvir 2.5-fold | Do not coadminister.  
Do not coadminister. |
| | TPV/r | ↑ glecaprevir and pibrentasvir expected | | |
| **Ledipasvir/ Sofosbuvir** | ATV/r | ATV AUC ↑ 33%  
Ledipasvir AUC ↑ 113%  
↔ sofosbuvir | No dose adjustment necessary.  
Coadministration of ledipasvir/sofosbuvir with TDF and a PI/r results in increased exposure to TDF. The safety of the increased TDF exposure has not been established. Consider alternative HCV or ARV drugs to avoid increased TDF toxicities. If coadministration is necessary, monitor for TDF-associated adverse reactions. |
| | DRV/r | DRV ↔ expected  
↔ ledipasvir/sofosbuvir | | |
<p>| | ATV (unboosted), ATV/c, DRV/c, LPV/r | ↔ expected | | |
| | TPV/r | ↓ ledipasvir and sofosbuvir expected | Do not coadminister. |</p>
<table>
<thead>
<tr>
<th>Hepatitis C Direct-Acting Antiviral Agents, continued</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Simeprevir</strong></td>
</tr>
<tr>
<td>All PIs</td>
</tr>
<tr>
<td>Do not coadminister.</td>
</tr>
<tr>
<td><strong>Sofosbuvir</strong></td>
</tr>
<tr>
<td>TPV/r</td>
</tr>
<tr>
<td>Do not coadminister.</td>
</tr>
<tr>
<td><strong>Sofosbuvir/ Velpatasvir</strong></td>
</tr>
<tr>
<td>ATV/r</td>
</tr>
<tr>
<td>↔ sofosbuvir</td>
</tr>
<tr>
<td>Velpatasvir AUC ↑ 2.4-fold</td>
</tr>
<tr>
<td>DRV/r</td>
</tr>
<tr>
<td>Sofosbuvir AUC ↓ 28%</td>
</tr>
<tr>
<td>↔ velpatasvir</td>
</tr>
<tr>
<td>ATV (unboosted), ATV/c, DRV/c, LPV/r</td>
</tr>
<tr>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td><strong>Sofosbuvir/ Velpatasvir/ Voxilaprevir</strong></td>
</tr>
<tr>
<td>ATV (unboosted), ATV/c, ATV/r</td>
</tr>
<tr>
<td>LPV/r</td>
</tr>
<tr>
<td>DRV/r, DRV/c</td>
</tr>
<tr>
<td>TPV/r</td>
</tr>
<tr>
<td>↓ velpatasvir expected</td>
</tr>
<tr>
<td>Effect on voxilaprevir is unknown</td>
</tr>
<tr>
<td>Do not coadminister.</td>
</tr>
</tbody>
</table>

**Herbal Products**

| St. John’s Wort | All PIs | ↓ PI expected | Contraindicated. |

**Hormonal Therapies**

| Hormonal Contraceptives Oral | ATV (unboosted) | Ethinyl estradiol AUC ↑ 48% Norethindrone AUC ↑ 110% | Prescribe oral contraceptive that contains no more than 30 mcg of ethinyl estradiol or recommend alternative contraceptive method. Oral contraceptives containing less than 25 mcg of ethinyl estradiol or progestins other than norethindrone or norgestimate have not been studied. |

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Table 18a. Drug Interactions Between Protease Inhibitors and Other Drugs *(Last updated October 17, 2017; last reviewed October 17, 2017)* (page 11 of 17)
### Concomitant Drug

### Hormonal Therapies, continued

<table>
<thead>
<tr>
<th>Concomitant Drug</th>
<th>PI</th>
<th>Effect on PI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hormonal Contraceptives</strong> <strong>Oral</strong></td>
<td>ATV/r</td>
<td>Ethinyl estradiol AUC ↓ 19% and C&lt;sub&gt;min&lt;/sub&gt; ↓ 37%</td>
<td>Oral contraceptive should contain at least 35 mcg of ethinyl estradiol. Only hormonal contraceptives containing progestins other than norethindrone or norgestimate have been studied.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Norgestimate ↑ 85%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Norethindrone AUC ↑ 51% and C&lt;sub&gt;min&lt;/sub&gt; ↑ 67%</td>
<td></td>
</tr>
<tr>
<td>ATV/c</td>
<td>Drospernone AUC ↑ 2.3-fold</td>
<td></td>
<td>Contraindicated with drospernone-containing hormonal contraceptive. Do not coadminister due to potential for hyperkalemia. Consider alternative contraceptive method or alternative ARV drug.</td>
</tr>
<tr>
<td></td>
<td>Ethinyl estradiol AUC ↓ 22%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DRV/c</td>
<td>Drospernone AUC ↑ 1.6-fold</td>
<td></td>
<td>Clinical monitoring is recommended due to the potential for hyperkalemia. Consider alternative contraceptive method or alternative ARV.</td>
</tr>
<tr>
<td></td>
<td>Ethinyl estradiol AUC ↓ 30%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DRV/r, LPV/r, TPV/r</td>
<td>Ethinyl estradiol AUC ↓ 37% to 55%</td>
<td></td>
<td>Consider alternative contraceptive method or alternative ARV drug.</td>
</tr>
<tr>
<td></td>
<td>Norethindrone AUC ↓ 14% to 34%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>With TPV/r: norethindrone AUC ↔</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Depot Medroxyprogesterone Acetate (MPA) Injectable</strong></td>
<td>LPV/r</td>
<td>MPA AUC ↑ 46%</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C&lt;sub&gt;min&lt;/sub&gt;: no significant change</td>
<td></td>
</tr>
<tr>
<td><strong>Etonogestrel-Releasing Subdermal Implant</strong></td>
<td>LPV/r</td>
<td>Etonogestrel AUC ↑ 52% and C&lt;sub&gt;min&lt;/sub&gt; ↑ 34%</td>
<td>Use standard dose.</td>
</tr>
<tr>
<td>All other PIs</td>
<td>No data</td>
<td>Consider alternative contraceptive method or alternative ARV drug.</td>
<td></td>
</tr>
<tr>
<td><strong>Transdermal Ethinyl Estradiol/Norelgestromin</strong></td>
<td>LPV/r</td>
<td>LPV ↔ Ethinyl estradiol AUC ↓ 45%, norelgestromin AUC ↑ 83%</td>
<td>Use standard dose.</td>
</tr>
<tr>
<td>All other PIs</td>
<td>No data</td>
<td>Consider alternative contraceptive method or alternative ARV drug.</td>
<td></td>
</tr>
<tr>
<td><strong>Menopausal Hormone Replacement Therapy</strong></td>
<td>All PIs</td>
<td>With estradiol or conjugated estrogen (equine and synthetic): ↓ estrogen possible</td>
<td>Adjust estrogen dosage as needed based on clinical effects.</td>
</tr>
<tr>
<td>All PIs</td>
<td>↑ drospernone possible</td>
<td>↑ medroxyprogesterone</td>
<td>Adjust progestin/progesterone dosage as needed based on clinical effects. Because drospernone is prescribed as a lower dose for menopausal HRT than the products used for hormonal contraceptives, it is not contraindicated with ATV/c products.</td>
</tr>
<tr>
<td></td>
<td>↑ micronized progesterone</td>
<td>See Hormonal Contraceptives for other progestin-PI interactions</td>
<td></td>
</tr>
</tbody>
</table>

---

**Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV**

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## Concomitant Drug

### Hormonal Therapies, continued

<table>
<thead>
<tr>
<th>Gender-Affirming Hormone Therapy</th>
<th>All PIs</th>
<th>Effect on PI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>↓ estradiol possible</td>
<td>Adjust estradiol dosage as needed based on clinical effects and endogenous hormone concentrations.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>↔ finasteride, goserelin, leuprolide acetate, and spironolactone expected</td>
<td>No dose adjustment necessary.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>↑ dutasteride possible</td>
<td>Adjust dutasteride dosage as needed based on clinical effects and endogenous hormone concentrations.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓ testosterone possible</td>
<td>Adjust testosterone dosage as needed based on clinical effects and endogenous hormone concentrations.</td>
<td></td>
</tr>
</tbody>
</table>

### HMG-CoA Reductase Inhibitors

#### Atorvastatin

<table>
<thead>
<tr>
<th>PI</th>
<th>Effect on Atorvastatin</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATV, ATV/r</td>
<td>↑ atorvastatin possible</td>
<td>Titrate atorvastatin dose carefully and use lowest dose necessary while monitoring for toxicities.</td>
</tr>
<tr>
<td>ATV/c</td>
<td>AUC ↑ 9.2-fold, C&lt;sub&gt;max&lt;/sub&gt; ↑ 18.9-fold</td>
<td>Coadministration is not recommended.</td>
</tr>
<tr>
<td>DRV/r</td>
<td>DRV/r + atorvastatin 10 mg similar to atorvastatin 40 mg administered alone</td>
<td>Titrate atorvastatin dose carefully and use the lowest dose necessary while monitoring for toxicities. Do not exceed 20 mg atorvastatin daily.</td>
</tr>
<tr>
<td>DRV/c</td>
<td>AUC ↑ 3.9-fold, C&lt;sub&gt;max&lt;/sub&gt; ↑ 4.2-fold</td>
<td>Titrate atorvastatin dose carefully and use lowest dose necessary while monitoring for toxicities. Do not exceed 20 mg atorvastatin daily.</td>
</tr>
<tr>
<td>LPV/r</td>
<td>AUC ↑ 5.9-fold, C&lt;sub&gt;max&lt;/sub&gt; ↑ 4.7-fold</td>
<td>Titrate atorvastatin dose carefully and use lowest dose necessary while monitoring for toxicities. Do not exceed 20 mg atorvastatin daily.</td>
</tr>
<tr>
<td>TPV/r</td>
<td>AUC ↑ 9.4-fold, C&lt;sub&gt;max&lt;/sub&gt; ↑ 8.6-fold</td>
<td>Do not coadminister.</td>
</tr>
</tbody>
</table>

#### Lovastatin

<table>
<thead>
<tr>
<th>PI</th>
<th>Effect on Lovastatin</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATV/c, ATV/r</td>
<td>No data</td>
<td>Titrate pravastatin dose carefully while monitoring for toxicities.</td>
</tr>
</tbody>
</table>
| DRV/c, DRV/r | With DRV/r, Pravastatin AUC:  
* ↑ 81% following single dose of pravastatin  
* ↑ 23% at steady state | Titrate pravastatin dose carefully while monitoring for toxicities. |
| LPV/r       | Pravastatin AUC ↑ 33% | No dose adjustment necessary. |
### HMG-CoA Reductase Inhibitors, continued

<table>
<thead>
<tr>
<th>Concomitant Drug</th>
<th>PI</th>
<th>Effect on PI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rosuvastatin</td>
<td>ATV/r</td>
<td>Rosuvastatin AUC ↑ 3-fold, C&lt;sub&gt;max&lt;/sub&gt; ↑ 7-fold</td>
<td>Titrate rosuvastatin dose carefully and use lowest dose necessary while monitoring for toxicities. Do not exceed 10 mg rosuvastatin daily.</td>
</tr>
<tr>
<td></td>
<td>ATV/c</td>
<td>Rosuvastatin AUC ↑ 3.4-fold, C&lt;sub&gt;max&lt;/sub&gt; ↑ 10.6-fold</td>
<td></td>
</tr>
<tr>
<td></td>
<td>DRV/c</td>
<td>Rosuvastatin AUC ↑ 1.9-fold, C&lt;sub&gt;max&lt;/sub&gt; ↑ 3.8-fold</td>
<td>Titrate rosuvastatin dose carefully and use the lowest necessary dose while monitoring for toxicities. Do not exceed 20 mg rosuvastatin daily.</td>
</tr>
<tr>
<td></td>
<td>DRV/r</td>
<td>Rosuvastatin AUC ↑ 48%, C&lt;sub&gt;max&lt;/sub&gt; ↑ 2.4-fold</td>
<td>Titrate rosuvastatin dose carefully and use the lowest necessary dose while monitoring for toxicities.</td>
</tr>
<tr>
<td></td>
<td>LPV/r</td>
<td>Rosuvastatin AUC ↑ 2.1-fold, C&lt;sub&gt;max&lt;/sub&gt; ↑ 4.7-fold</td>
<td>Titrate rosuvastatin dose carefully and use the lowest necessary dose. Do not exceed 10 mg rosuvastatin daily.</td>
</tr>
<tr>
<td></td>
<td>TPV/r</td>
<td>Rosuvastatin AUC ↑ 26%, C&lt;sub&gt;max&lt;/sub&gt; ↑ 2.2-fold</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>All PIs</td>
<td>Significant ↑ simvastatin expected</td>
<td>Contraindicated.</td>
</tr>
</tbody>
</table>

### Immunosuppressants

<table>
<thead>
<tr>
<th>Therapy</th>
<th>All PIs</th>
<th>Effect on Immunosuppressant</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclosporine, Everolimus, Sirolimus, Tacrolimus</td>
<td>↑ immunosuppressant expected</td>
<td>Initiate with an adjusted dose of immunosuppressant to account for potential increased concentrations of the immunosuppressant and monitor for toxicities. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with specialist as necessary.</td>
<td></td>
</tr>
</tbody>
</table>

### Narcotics and Treatment for Opioid Dependence

<table>
<thead>
<tr>
<th>Therapy</th>
<th>ATV (unboosted)</th>
<th>ATV/r</th>
<th>ATV/c, DRV/c</th>
<th>DRV/r</th>
<th>LPV/r</th>
<th>TPV/r</th>
<th>Effect on Buprenorphine</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
<td>Buprenorphine AUC ↑ 93%</td>
<td>Buprenorphine AUC ↑ 66%</td>
<td>Effects unknown</td>
<td>Buprenorphine: no significant effect</td>
<td>No significant effect</td>
<td>Buprenorphine: no significant effect</td>
<td>Do not coadminister buprenorphine with unboosted ATV. Monitor for sedation and other signs or symptoms of over-medication. Buprenorphine dose reduction may be necessary. It may be necessary to remove implant and treat with a formulation that permits dose adjustments. Titrate buprenorphine dose using the lowest initial dose. Dose adjustment of buprenorphine may be needed. It may be necessary to remove implant and treat with a formulation that permits dose adjustments. Clinical monitoring is recommended. No dose adjustment necessary. Clinical monitoring is recommended. When transferring buprenorphine from transmucosal to implantation, monitor to ensure buprenorphine effect is adequate and not excessive. Consider monitoring TPV level. When transferring buprenorphine from transmucosal to implantation, monitor to ensure buprenorphine effect is adequate and not excessive.</td>
<td></td>
</tr>
<tr>
<td>Sublingual, buccal, or implant</td>
<td>Norbuprenorphine&lt;sup&gt;a&lt;/sup&gt; AUC ↑ 76%</td>
<td>Norbuprenorphine&lt;sup&gt;a&lt;/sup&gt; AUC ↑ 105%</td>
<td></td>
<td>Buprenorphine: no significant effect</td>
<td>No significant effect</td>
<td>Buprenorphine: no significant effect</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓ ATV possible</td>
<td></td>
<td></td>
<td>Buprenorphine: no significant effect</td>
<td>No significant effect</td>
<td>Buprenorphine: no significant effect</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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*Table 18a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017)* (page 14 of 17)
### Narcotics and Treatment for Opioid Dependence, continued

<table>
<thead>
<tr>
<th>Concomitant Drug</th>
<th>PI</th>
<th>Effect on PI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl</td>
<td>All PIs</td>
<td>↑ fentanyl possible</td>
<td>Clinical monitoring is recommended, including for potentially fatal respiratory depression.</td>
</tr>
<tr>
<td>Methadone</td>
<td>ATV (unboosted)</td>
<td>No significant effect</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td>ATV/c, DRV/c</td>
<td>Effects unknown</td>
<td>Titrate methadone dose using the lowest feasible initial dose. Dose adjustment of methadone may be needed. Clinical monitoring is recommended.</td>
</tr>
<tr>
<td>All PI/r</td>
<td>ATV/r and DRV/r ↓</td>
<td>R-methadone AUC 16%–18%</td>
<td>Opioid withdrawal is unlikely but may occur. Dosage adjustment of methadone is not usually required, but monitor for opioid withdrawal and increase methadone dose as clinically indicated.</td>
</tr>
<tr>
<td>Methadone</td>
<td>All PIs</td>
<td>Oxycodone AUC ↑ 2.6-fold with LPV/r</td>
<td>Monitor for opioid-related adverse effects. Oxycodone dose reduction may be necessary.</td>
</tr>
<tr>
<td>Tramadol</td>
<td>ATV/c, DRV/c</td>
<td>↑ tramadol possible</td>
<td>Tramadol dose reduction may be necessary. Monitor for tramadol toxicities and clinical response.</td>
</tr>
</tbody>
</table>

### Phosphodiesterase Type 5 (PDE5) Inhibitors

<table>
<thead>
<tr>
<th>Concomitant Drug</th>
<th>PI</th>
<th>Effect on PI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avanafil</td>
<td>All PIs except unboosted ATV</td>
<td>RTV (600 mg BID for 5 days) ↑ avanafil AUC 13-fold, C_max 2.4-fold</td>
<td>Coadministration is not recommended.</td>
</tr>
<tr>
<td></td>
<td>ATV (unboosted)</td>
<td>No data</td>
<td>Avanafil dose should not exceed 50 mg once every 24 hours.</td>
</tr>
<tr>
<td>Sildenafil</td>
<td>All PIs</td>
<td>DRV/r + sildenafil 25 mg similar to sildenafil 100 mg alone</td>
<td>For Treatment of Erectile Dysfunction:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RTV 500 mg BID ↑ sildenafil AUC 1000%</td>
<td>• Start with sildenafil 25 mg every 48 hours and monitor for adverse effects of sildenafil.</td>
</tr>
<tr>
<td>Tadalafil</td>
<td>All PIs</td>
<td>RTV 200 mg BID ↑ tadalafil AUC 124%</td>
<td>For Treatment of Erectile Dysfunction:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TPV/r (1st dose) ↑ tadalafil AUC 133%</td>
<td>• Start with tadalafil 5-mg dose and do not exceed a single dose of 10 mg every 72 hours. Monitor for adverse effects of tadalafil.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TPV/r steady state: no significant effect</td>
<td>For Treatment of PAH:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Contraindicated.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>In patients on a PI &gt;7 days:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Start with tadalafil 20 mg once daily and increase to 40 mg once daily based on tolerability.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>In patients on tadalafil who require a PI:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Stop tadalafil ≥24 hours before PI initiation. Seven days after PI initiation, restart tadalafil at 20 mg once daily and increase to 40 mg once daily based on tolerability.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>In patients switching between COBI and RTV:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Maintain tadalafil dose.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>For Treatment of Benign Prostatic Hyperplasia:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Maximum recommended daily dose is 2.5 mg per day.</td>
</tr>
</tbody>
</table>
Table 18a. Drug Interactions Between Protease Inhibitors and Other Drugs  
(Last updated October 17, 2017; last reviewed October 17, 2017)  
(page 16 of 17)

<table>
<thead>
<tr>
<th>Concomitant Drug</th>
<th>PI</th>
<th>Effect on PI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Phosphodiesterase Type 5 (PDE5) Inhibitors, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vardenafil</td>
<td>All PIs</td>
<td>RTV 600 mg BID ↑ vardenafil AUC 49-fold</td>
<td>Start with vardenafil 2.5 mg every 72 hours and monitor for adverse effects of vardenafil.</td>
</tr>
<tr>
<td><strong>Sedative/Hypnotics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alprazolam, Clonazepam, Diazepam</td>
<td>All PIs</td>
<td>↑ benzodiazepine possible RTV (200 mg BID for 2 days) ↑ alprazolam half-life 222% and AUC 248%</td>
<td>Consider alternative benzodiazepines such as lorazepam, oxazepam, or temazepam.</td>
</tr>
<tr>
<td>Lorazepam, Oxazepam, Temazepam</td>
<td>All PIs</td>
<td>No data</td>
<td>These benzodiazepines are metabolized via non-CYP450 pathways; thus, there is less interaction potential than with other benzodiazepines.</td>
</tr>
<tr>
<td>Midazolam</td>
<td>All PIs</td>
<td>↑ midazolam expected</td>
<td>Do not coadminister oral midazolam and PIs. Parenteral midazolam can be used with caution when given as a single dose in a monitored situation for procedural sedation.</td>
</tr>
<tr>
<td>Suvorexant</td>
<td>All PIs</td>
<td>↑ suvorexant expected</td>
<td>Coadministration is not recommended.</td>
</tr>
<tr>
<td>Triazolam</td>
<td>All PIs</td>
<td>↑ triazolam expected RTV (200 mg BID) ↑ triazolam half-life 1200% and AUC 2000%</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td>Zolpidem</td>
<td>PI/r, ATV/c, DRV/c</td>
<td>↑ zolpidem possible</td>
<td>Initiate zolpidem at a low dose. Dose reduction may be necessary.</td>
</tr>
<tr>
<td><strong>Miscellaneous Drugs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alfuzosin</td>
<td>All PIs</td>
<td>↑ alfuzosin expected</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td>Calcifediol</td>
<td>All PIs</td>
<td>↑ calcifediol possible</td>
<td>Dose adjustment of calcifediol may be required, and serum 25-hydroxyvitamin D, intact PTH, and serum calcium concentrations should be closely monitored.</td>
</tr>
<tr>
<td>Cisapride</td>
<td>All PIs</td>
<td>↑ cisapride expected</td>
<td>Contraindicated.</td>
</tr>
</tbody>
</table>
| Colchicine | All PIs | RTV 100 mg BID ↑ colchicine AUC 296%, Cmax 184% With all PIs with or without COBI or RTV: significant ↑ colchicine expected | For Treatment of Gout Flares:  
- Colchicine 0.6 mg x 1 dose, followed by 0.3 mg 1 hour later. Do not repeat dose for at least 3 days.  
For Prophylaxis of Gout Flares:  
- Colchicine 0.3 mg once daily or every other day.  
For Treatment of Familial Mediterranean Fever:  
- Do not exceed colchicine 0.6 mg once daily or 0.3 mg BID.  
Do not coadminister in patients with hepatic or renal impairment. |
| Dronabinol | All PIs | ↑ dronabinol possible | Monitor for increased dronabinol-related adverse reactions. |
| Eluxadoline | All PIs | ↑ eluxadoline expected | Administer eluxadoline at a dose of 75 mg twice daily and monitor for eluxadoline-related adverse effects. |
| Ergot Derivatives | All PIs | ↑ dihydroergotamine, ergotamine, methylergonovine expected | Contraindicated. |
### Table 18a. Drug Interactions Between Protease Inhibitors and Other Drugs

(Updated October 17, 2017; last reviewed October 17, 2017)

<table>
<thead>
<tr>
<th>Concomitant Drug</th>
<th>PI</th>
<th>Effect on PI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Miscellaneous Drugs, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flibanserin</td>
<td>All PIs</td>
<td>↑ flibanserin expected</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td>Irinotecan</td>
<td>ATV, ATV/c, ATV/r</td>
<td>↑ irinotecan expected</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td>Salmeterol</td>
<td>All PIs</td>
<td>↑ salmeterol possible</td>
<td>Do not coadminister because of potential increased risk of salmeterol-associated CV events.</td>
</tr>
</tbody>
</table>

* DHA is an active metabolite of artemether.

* The following products contain at least 35 mcg of ethinyl estradiol combined with norethindrone or norgestimate (generic formulation may also be available): Brevicon; Femcon Fe; Modicon; Norinyl 1/35; Ortho-Cyclen; Ortho-Novum 1/35, 7/7/7; Ortho Tri-Cyclen; Ovcon 35; Tri-Norinyl.

* The following products contain no more than 30 mcg of ethinyl estradiol combined with norethindrone or norgestimate (generic formulation may also be available): Lo Minastrin Fe; Lo Loestrin Fe; Loestrin 1/20, 1.5/30; Loestrin Fe 1/20, 1.5/30; Loestrin 24 Fe; Minastrin 24 Fe; Ortho Tri-Cyclen Lo.

* Norbuprenorphine is an active metabolite of buprenorphine.

* R-methadone is the active form of methadone.

**Key to Symbols:**

↑ = increase

↓ = decrease

↔ = no change

**Key to Acronyms:**

17-BMP = beclomethasone 17-monopropionate; ALT = alanine aminotransferase; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BID = twice daily; C<sub>max</sub> = maximum plasma concentration; C<sub>min</sub> = minimum plasma concentration; CNS = central nervous system; COBI, c = cobicistat; CrCl = creatinine clearance; CV = cardiovascular; CYP = cytochrome P; DHA = dihydroartemisinin; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; ECG = electrocardiogram; eGFR = estimated glomerular filtration rate; HCV = hepatitis C virus; HRT = hormone replacement therapy; INR = international normalized ratio; LPV = lopinavir; LPV/r = ritonavir-boosted lopinavir; MPA = medroxyprogesterone acetate; P AH = pulmonary arterial hypertension; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; PK = pharmacokinetic; PPI = proton pump inhibitor; PTH = parathyroid hormone; QTc = QT corrected for heart rate; RTV, r = ritonavir; TCA = tricyclic antidepressant; TDF = tenofovir disoproxil fumarate; TPV = tipranavir; TPV/r = tipranavir/ritonavir; VPA = valproic acid
Table 18b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 1 of 9)

This table provides information relating to PK interactions between NNRTIs and non-ARV drugs. For interactions between ARV agents and for dosing recommendations, refer to Tables 18c, 19a, and 19b.

Recommendations for managing a particular drug interaction may differ depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or if a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly.

Note: Delavirdine (DLV) is not included in this table. Please refer to the DLV Food and Drug Administration package insert for information regarding drug interactions.

<table>
<thead>
<tr>
<th>Concomitant Drug Class/ Name</th>
<th>NNRTI(^a)</th>
<th>Effect on NNRTI and/ or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acid Reducers</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antacids</td>
<td>RPV</td>
<td>↓ RPV expected when given simultaneously</td>
<td>Give antacids at least 2 hours before or at least 4 hours after RPV.</td>
</tr>
<tr>
<td>H2 Receptor Antagonists</td>
<td>RPV</td>
<td>↓ RPV</td>
<td>Give H2 receptor antagonists at least 12 hours before or at least 4 hours after RPV.</td>
</tr>
<tr>
<td>PPIs</td>
<td>RPV</td>
<td>With Omeprazole 20 mg Daily:</td>
<td>Contraindicated. Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• RPV AUC ↓ 40%, C(_{\text{min}}) ↓ 33%</td>
<td></td>
</tr>
<tr>
<td><strong>Anticoagulants/Antiplatelets</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apixaban</td>
<td>EFV, ETR, NVP</td>
<td>↓ apixaban possible</td>
<td>Consider alternative therapy.</td>
</tr>
<tr>
<td>Betrixaban</td>
<td>EFV, NVP, RPV</td>
<td>↔ betrixaban expected</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>↑ betrixaban possible</td>
<td>Consider alternative therapy. If coadministration is necessary, reduce betrixaban initial dose to 80 mg, followed by 40 mg daily. Monitor for betrixaban toxicity.</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>ETR</td>
<td>↓ activation of clopidogrel possible</td>
<td>ETR may prevent metabolism of clopidogrel (inactive) to its active metabolite. Avoid coadministration, if possible.</td>
</tr>
<tr>
<td></td>
<td>NVP, RPV</td>
<td>↔ clopidogrel expected</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Dabigatran</td>
<td>EFV, NVP, RPV</td>
<td>↔ dabigatran expected</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>↑ dabigatran possible</td>
<td>Consider alternative therapy. If coadministration is necessary, monitor for dabigatran toxicity.</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>EFV, NVP, RPV</td>
<td>↔ edoxaban expected</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>↑ edoxaban possible</td>
<td>Consider alternative therapy. If coadministration is necessary, monitor for edoxaban toxicity.</td>
</tr>
<tr>
<td>Prasugrel</td>
<td>EFV, ETR, NVP</td>
<td>↔ prasugrel expected</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>EFV, ETR, NVP</td>
<td>↓ rivaroxaban possible</td>
<td>Consider alternative therapy.</td>
</tr>
<tr>
<td>Ticagrelor</td>
<td>EFV, ETR, NVP</td>
<td>↓ ticagrelor expected</td>
<td>Consider alternative therapy.</td>
</tr>
<tr>
<td>Warfarin</td>
<td>EFV, ETR, NVP</td>
<td>↑ or ↓ warfarin possible</td>
<td>Monitor INR and adjust warfarin dose accordingly.</td>
</tr>
<tr>
<td>Concomitant Drug Class/ Name</td>
<td>NNRTI</td>
<td>Effect on NNRTI and/or Concomitant Drug Concentrations</td>
<td>Dosing Recommendations and Clinical Comments</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>-------</td>
<td>-------------------------------------------------------</td>
<td>---------------------------------------------</td>
</tr>
<tr>
<td><strong>Anticonvulsants</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbamazepine, Phenobarbital, Phenytin</td>
<td>EFV, ETR, NVP, RPV</td>
<td>↓ NNRTI possible</td>
<td>Monitor virologic outcomes and consider monitoring plasma concentrations of ARVs, or consider alternative anticonvulsant or ARV drug.</td>
</tr>
<tr>
<td>Ethosuximide, Lacosamide, Tiagabine, Zonisamide</td>
<td>ETR, EFV</td>
<td>↓ anticonvulsant possible</td>
<td>Monitor seizure control and plasma concentrations of anticonvulsants (when available).</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>EFV</td>
<td>↓ lamotrigine possible</td>
<td>Monitor seizure control and plasma concentrations of lamotrigine.</td>
</tr>
<tr>
<td><strong>Antidepressants</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bupropion</td>
<td>EFV, NVP</td>
<td>Bupropion AUC ↓ 55% ↓ bupropion possible</td>
<td>Titrate bupropion dose based on clinical response.</td>
</tr>
<tr>
<td>Citalopram, Escitalopram</td>
<td>EFV, ETR, NVP</td>
<td>↓ antidepressant possible</td>
<td>Titrate antidepressant dose based on clinical response.</td>
</tr>
<tr>
<td>Fluoxetine, Fluvoxamine</td>
<td>EFV, ETR, NVP, RPV</td>
<td>↔ antidepressant expected</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>EFV, ETR, NVP, RPV</td>
<td>↔ paroxetine observed with EFV or ETR ↔ expected with NVP or RPV</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Nefazodone</td>
<td>EFV, ETR, NVP, RPV</td>
<td>↓ nefazodone expected ↓ NNRTI possible ↑ RPV possible</td>
<td>Monitor the antidepressant effect and titrate dose as necessary. Monitor for ARV-related adverse events.</td>
</tr>
<tr>
<td>Sertraline</td>
<td>EFV</td>
<td>Sertraline AUC ↓ 39%</td>
<td>Titrate sertraline dose based on clinical response.</td>
</tr>
<tr>
<td>Trazodone</td>
<td>EFV, ETR, NVP</td>
<td>↓ trazodone possible</td>
<td>Monitor the therapeutic effect of trazodone and titrate dose as necessary.</td>
</tr>
</tbody>
</table>
Table 18b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs *(Last updated October 17, 2017; last reviewed October 17, 2017)* (page 3 of 9)

<table>
<thead>
<tr>
<th>Concomitant Drug Class/ Name</th>
<th>NNRTI&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Effect on NNRTI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antifungals</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluconazole</td>
<td>EFV</td>
<td>↔ fluconazole or EFV</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>ETR AUC ↑ 86%</td>
<td>No dose adjustment necessary. Use with caution.</td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>NVP AUC ↑ 110%</td>
<td>Increased risk of hepatotoxicity possible with this combination. Monitor NVP toxicity or use alternative ARV agent.</td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>↑ RPV possible</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Isavuconazole</td>
<td>EFV, ETR, NVP</td>
<td>↓ isavuconazole possible</td>
<td>Dose adjustments for isavuconazole may be necessary. Consider monitoring isavuconazole level and antifungal response.</td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>↑ RPV possible</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Itraconazole</td>
<td>EFV</td>
<td>Itraconazole and OH-itraconazole AUC, C&lt;sub&gt;max&lt;/sub&gt;, and C&lt;sub&gt;min&lt;/sub&gt; ↓ 35%–44%</td>
<td>Failure to achieve therapeutic itraconazole concentrations has been reported. Avoid this combination if possible. If coadministered, closely monitor itraconazole concentration and adjust dose accordingly.</td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>↓ itraconazole possible</td>
<td>Dose adjustments for itraconazole may be necessary. Monitor itraconazole level and antifungal response.</td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>↑ ETR possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>Itraconazole AUC ↓ 61%</td>
<td>Avoid this combination if possible. If coadministered, monitor itraconazole concentration and adjust dose accordingly.</td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>↑ NVP possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>↑ RPV possible</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Posaconazole</td>
<td>EFV</td>
<td>Posaconazole AUC ↓ 50%</td>
<td>Avoid concomitant use unless the benefit outweighs the risk. If coadministered, monitor posaconazole concentration and adjust dose accordingly.</td>
</tr>
<tr>
<td></td>
<td>ETR, NVP, RPV</td>
<td>↑ NNRTI possible</td>
<td>Monitor for NNRTI toxicities.</td>
</tr>
<tr>
<td>Voriconazole</td>
<td>EFV</td>
<td>Voriconazole AUC ↓ 77%</td>
<td>Contraindicated at standard doses.</td>
</tr>
<tr>
<td></td>
<td>EFV</td>
<td>EFV AUC ↑ 44%</td>
<td>Dose Adjustment:</td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>Voriconazole AUC ↑ 14%</td>
<td>• Voriconazole 400 mg BID, EFV 300 mg daily</td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>ETR AUC ↑ 36%</td>
<td>No dose adjustment necessary; use with caution. Consider monitoring voriconazole level.</td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>↓ voriconazole possible</td>
<td>Monitor for toxicity and antifungal response and/or voriconazole level.</td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>↑ NVP possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>↑ RPV possible</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td><strong>Antihyperglycemics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canagliflozin, Dapagliflozin, Empagliflozin, Sitagliptin</td>
<td>EFV, ETR, NVP, RPV</td>
<td>↔ antihyperglycemic expected</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Linagliptin, Saxagliptin</td>
<td>EFV, ETR, NVP</td>
<td>↓ antihyperglycemic possible</td>
<td>Monitor glycemic control.</td>
</tr>
<tr>
<td>Concomitant Drug Class/Name</td>
<td>NNRTI&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Effect on NNRTI and/or Concomitant Drug Concentrations</td>
<td>Dosing Recommendations and Clinical Comments</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>-------------------</td>
<td>------------------------------------------------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td><strong>Antimalarials</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Artemether/ Lumefantrine</td>
<td>EFV</td>
<td>Artemether AUC ↓ 79%</td>
<td>Consider alternative ARV or antimalarial drug. If used in combination, monitor closely for antimalarial efficacy and malaria recurrence.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DHA AUC ↓ 75%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lumefantrine AUC ↓ 56%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>Artemether AUC ↓ 38%</td>
<td>Clinical significance of the reduced antimalarial drug concentrations unknown. If used in combination with ETR, monitor closely for antimalarial efficacy.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DHA AUC ↓ 15%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lumefantrine AUC ↓ 13%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>ETR AUC ↑ 10%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>Artemether AUC ↓ 67%–72%</td>
<td>Clinical significance unknown. If used, monitor closely for antimalarial efficacy and lumefantrine toxicity.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DHA:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Study results are conflicting. AUC ↓ 37% in one study, no difference in another.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lumefantrine:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Study results are conflicting. Lumefantrine AUC ↓ 25%–58% in 2 studies but ↑ 56% in another.</td>
<td></td>
</tr>
<tr>
<td>Atovaquone/ Proguanil</td>
<td>EFV</td>
<td>Atovaquone AUC ↓ 75%</td>
<td>No dose recommendation. Consider alternative drug for malaria prophylaxis, if possible.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Proguanil AUC ↓ 43%</td>
<td></td>
</tr>
<tr>
<td><strong>Antimycobacterials</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bedaquiline</td>
<td>EFV, ETR</td>
<td>↓ bedaquiline possible</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>↔ bedaquiline AUC</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>EFV</td>
<td>Clarithromycin AUC ↓ 39%</td>
<td>Monitor for effectiveness or consider alternative agent, such as azithromycin, for MAC prophylaxis and treatment.</td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>Clarithromycin AUC ↓ 39%</td>
<td>Consider alternative agent, such as azithromycin, for MAC prophylaxis and treatment.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ETR AUC ↑ 42%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>Clarithromycin AUC ↓ 31%</td>
<td>Monitor for effectiveness or use alternative agent, such as azithromycin, for MAC prophylaxis and treatment.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NVP AUC ↑ 26%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>↔ clarithromycin expected</td>
<td>Consider alternative macrolide, such as azithromycin, for MAC prophylaxis and treatment.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ RPV possible</td>
<td></td>
</tr>
<tr>
<td>Rifabutin</td>
<td>EFV</td>
<td>Rifabutin ↓ 38%</td>
<td>Dose:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Rifabutin 450–600 mg/day; or</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Rifabutin 600 mg 3 times/week if EFV is not coadministered with a PI.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>Rifabutin and metabolite AUC ↓ 17%</td>
<td>If ETR is used with an RTV-boosted PI, rifabutin should not be coadministered.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ETR AUC ↓ 37%</td>
<td>Dose:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Rifabutin 300 mg once daily if ETR is not coadministered with a PI.</td>
<td></td>
</tr>
</tbody>
</table>
### Table 18b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

**Antimycobacterials**

<table>
<thead>
<tr>
<th>Concomitant Drug Class/ Name</th>
<th>NNRTI</th>
<th>Effect on NNRTI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifabutin, continued</td>
<td>NVP</td>
<td>Rifabutin AUC ↑ 17% and metabolite AUC ↑ 24%</td>
<td>No dose adjustment necessary. Use with caution.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NVP C&lt;sub&gt;min&lt;/sub&gt; ↓ 16%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>Rifabutin + RPV 50 mg once daily compared to RPV 25 mg once daily alone: ↔ RPV AUC, C&lt;sub&gt;min&lt;/sub&gt;</td>
<td>Increase RPV dose to 50 mg once daily.</td>
</tr>
</tbody>
</table>

**Rifampin**

<p>| | | | | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>EFV</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>EFV AUC ↓ 26%</td>
<td>Maintain EFV dose at 600 mg once daily and monitor for virologic response. Consider therapeutic drug monitoring.</td>
</tr>
<tr>
<td>ETR</td>
<td></td>
<td></td>
<td>Significant ↓ ETR possible</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td>NVP</td>
<td></td>
<td></td>
<td>NVP ↓ 20%–58%</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td>RPV</td>
<td></td>
<td></td>
<td>RPV AUC ↓ 80%</td>
<td>Contraindicated. Do not coadminister.</td>
</tr>
</tbody>
</table>

**Rifapentine**

<p>| | | | | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>EFV</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>↔ EFV concentrations</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>ETR, NVP, RPV</td>
<td></td>
<td></td>
<td>↓ NNRTI possible</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td>RPV</td>
<td></td>
<td></td>
<td>↓ RPV expected</td>
<td>Contradindicated.</td>
</tr>
</tbody>
</table>

**Antipneumocystis and Antitoxoplasmosis Drugs**

<p>| | | | | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Atovaquone</td>
<td>Consider alternative agent for PCP or toxoplasmosis treatment or use alternative ARV drug. If used in combination, monitor therapeutic efficacy of atovaquone.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Atovaquone AUC ↓ 44%–47%</td>
<td></td>
</tr>
</tbody>
</table>

**Antipsychotics**

<p>| | | | | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Olanzapine</td>
<td>Monitor effect of olanzapine.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>↓ olanzapine possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>↔ olanzapine expected</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ETR, NVP, RPV</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pimozide</td>
<td>Coadministration is not recommended. Consider alternative antipsychotic.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>↑ pimozide possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ETR, NVP</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>↓ pimozide possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lurasidone, Quetiapine, Thioridazine</td>
<td>Monitor effect of antipsychotic.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>EFV, ETR, NVP</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>↓ antipsychotic possible</td>
<td></td>
</tr>
</tbody>
</table>

**Benzodiazepines**

<p>| | | | | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Alprazolam</td>
<td>Monitor for therapeutic effectiveness of alprazolam.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>EFV, ETR, NVP</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>↓ alprazolam possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Diazepam</td>
<td>Monitor for therapeutic effectiveness of diazepam.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>EFV, NVP</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>↓ diazepam possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ETR</td>
<td>Decreased dose of diazepam may be necessary. Monitor for diazepam toxicity.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>↑ diazepam possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lorazepam</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>EFV</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lorazepam C&lt;sub&gt;max&lt;/sub&gt; ↑ 16%, AUC ↔</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Midazolam</td>
<td>Do not coadminister with oral midazolam. Parenteral midazolam can be used with caution as a single dose and can be given in a monitored situation for procedural sedation.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>EFV</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Significant ↑ midazolam expected</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Triazolam</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>EFV</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Significant ↑ triazolam expected</td>
<td></td>
</tr>
<tr>
<td>Concomitant Drug Class/ Name</td>
<td>NNRTI (^a)</td>
<td>Effect on NNRTI and/or Concomitant Drug Concentrations</td>
<td>Dosing Recommendations and Clinical Comments</td>
<td></td>
</tr>
<tr>
<td>-----------------------------</td>
<td>-------------</td>
<td>-----------------------------------------------------</td>
<td>-------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Cardiac Medications</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dihydropyridine CCBs</td>
<td>EFV, ETR, NVP</td>
<td>↓ CCBs possible</td>
<td>Titrate CCB dose based on clinical response.</td>
<td></td>
</tr>
<tr>
<td>Diltiazem, Verapamil</td>
<td>EFV</td>
<td>Diltiazem AUC ↓ 69%</td>
<td>Titrate diltiazem or verapamil dose based on clinical response.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>↓ verapamil possible</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ diltiazem or verapamil possible</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corticosteroids</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>EFV, ETR, NVP</td>
<td>↓ EFV, ETR, and NVP possible</td>
<td>Consider alternative corticosteroid for long-term use. If dexamethasone is used with NNRTI, monitor virologic response.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>Significant ↓ RPV possible</td>
<td>Contraindicated with more than a single dose of dexamethasone.</td>
<td></td>
</tr>
<tr>
<td>Hepatitis C Direct-Acting Antiviral Agents</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daclatasvir</td>
<td>EFV, ETR, NVP</td>
<td>Daclatasvir 120 mg once daily + Daclatasvir 60 mg daily compared to daclatasvir 60 mg alone: daclatasvir C(_{\text{min}}) ↓ 17%, AUC ↑ 37%</td>
<td>The recommended dose is daclatasvir 90 mg once daily.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>No data</td>
<td>No dose adjustment necessary.</td>
<td></td>
</tr>
<tr>
<td>Dasabuvir + Paritaprevir/ Ombitasivir/RTV</td>
<td>EFV</td>
<td>No data</td>
<td>Contraindicated.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ETR, NVP</td>
<td>↓ DAAs possible</td>
<td>Do not coadminister.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>RPV AUC ↑ 150%–225%</td>
<td>Do not coadminister, due to potential for QT interval prolongation with higher concentrations of RPV.</td>
<td></td>
</tr>
<tr>
<td>Elbasvir/ Grazoprevir</td>
<td>EFV</td>
<td>Elbasvir AUC ↓ 54%</td>
<td>Contraindicated.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ETR, NVP</td>
<td>Grazoprevir AUC ↓ 83%</td>
<td>Do not coadminister.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>Elbasvir, grazoprevir expected</td>
<td>No dose adjustment necessary.</td>
<td></td>
</tr>
<tr>
<td>Glecaprevir/ Pibrentasvir</td>
<td>EFV</td>
<td>↓ glecaprevir and pibrentasvir expected</td>
<td>Do not coadminister.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NVP, ETR</td>
<td>↓ glecaprevir and pibrentasvir possible</td>
<td>No dose adjustment necessary.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>↓ glecaprevir, pibrentasvir, and RPV ↔</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ledipasvir/ Sofosbuvir</td>
<td>EFV</td>
<td>Ledipasvir AUC, C(<em>{\text{min}}), and C(</em>{\text{max}}) all ↓ 34%</td>
<td>No dose adjustment necessary.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ETR, NVP</td>
<td>No significant effect expected</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>Ledipasvir, sofosbuvir, and RPV ↔</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

\(^a\) NNRTI: Non-Nucleoside Reverse Transcriptase Inhibitors

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV

Downloaded from [https://aidsinfo.nih.gov/guidelines](https://aidsinfo.nih.gov/guidelines) on 8/8/2018
<table>
<thead>
<tr>
<th>Concomitant Drug Class/ Name</th>
<th>NNRTIa</th>
<th>Effect on NNRTI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hepatitis C Direct-Acting Antiviral Agents</strong>, continued</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simeprevir</td>
<td>EFV</td>
<td>Simeprevir AUC ↓ 71%, C\textsubscript{min} ↓ 91% ↔ EFV simeprevir expected</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td>ETR, NVP</td>
<td>↓ simeprevir expected</td>
<td>Do not coadminister.</td>
<td></td>
</tr>
<tr>
<td>RPV</td>
<td>↔ simeprevir and RPV</td>
<td>No dose adjustment necessary.</td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir/ Velpatasvir</td>
<td>EFV</td>
<td>Velpatasvir AUC ↓ 43%, C\textsubscript{max} ↓ 37% and C\textsubscript{min} ↓ 47%</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td>ETR, NVP</td>
<td>↓ velpatasvir expected</td>
<td>Do not coadminister.</td>
<td></td>
</tr>
<tr>
<td>RPV</td>
<td>No significant effect expected</td>
<td>No dose adjustment necessary.</td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir/ Velpatasvir/ Voxilaprevir</td>
<td>EFV</td>
<td>Velpatasvir AUC ↓ 43%, C\textsubscript{max} ↓ 37% and C\textsubscript{min} ↓ 47% ↔ voxilaprevir expected</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td>ETR, NVP</td>
<td>↓ voxilaprevir expected</td>
<td>Do not coadminister.</td>
<td></td>
</tr>
<tr>
<td>RPV</td>
<td>No significant effect expected</td>
<td>No dose adjustment necessary.</td>
<td></td>
</tr>
<tr>
<td><strong>Herbal Products</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>St. John’s Wort</td>
<td>EFV, ETR, NVP, RPV</td>
<td>↓ NNRTI</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td><strong>Hormonal Therapies</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hormonal Contraceptives</strong></td>
<td>EFV</td>
<td>Ethinyl estradiol ↔ Ethinyl estradiol AUC ↓ 83%</td>
<td>Use alternative or additional contraceptive methods.</td>
</tr>
<tr>
<td>Levonordestrol (metabolite of oral norgestimate) AUC ↓ 83%</td>
<td>Unintended pregnancies were observed in women who used EFV and levonordestrol implant concomitantly.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Norelgestromin (metabolite of oral norgestimate) AUC ↓ 64%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Etonogestrel (metabolite of oral desogestrel) C\textsubscript{max} ↓ 61%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Etonogestrol (implant) AUC ↓ 63%–82%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levonordestrol (implant) AUC ↓ 47%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DMPA: no significant change</td>
<td>No dose adjustment necessary.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ETR</td>
<td>Ethinyl estradiol AUC ↑ 22%</td>
<td>No dose adjustment necessary.</td>
<td></td>
</tr>
<tr>
<td>Norethindrone: no significant effect</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NVP</td>
<td>Ethinyl estradiol AUC ↓ 29%, C\textsubscript{max} ↓ 58%</td>
<td>Based on clinical data demonstrating no change in effectiveness, no dose adjustment necessary.</td>
<td></td>
</tr>
<tr>
<td>Norethindrone AUC ↓ 18%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Etonogestrol (metabolite of oral desogestrel) C\textsubscript{max} ↓ 22%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Etonogestrol (implant): no significant change</td>
<td>No dose adjustment necessary.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DMPA: no significant change</td>
<td>No dose adjustment necessary.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Table 18b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 8 of 9)

<table>
<thead>
<tr>
<th>Concomitant Drug Class/Name</th>
<th>NNRTI</th>
<th>Effect on NNRTI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hormonal Therapies, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hormonal Contraceptives, continued</td>
<td>NVP, continued</td>
<td>Levonorgestrel (implant) AUC ↑ 35%</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>Ethinyl estradiol: no significant change</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td>Norethindrone: no significant change</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levonorgestrel For emergency contraception</td>
<td>EFV</td>
<td>Levonorgestrel AUC ↓ 58%</td>
<td>Effectiveness of emergency postcoital contraception may be diminished.</td>
</tr>
<tr>
<td><strong>Menopausal Hormone Replacement Therapy</strong></td>
<td>EFV, ETR, NVP</td>
<td>With estradiol or conjugated estrogen (equine and synthetic): ↓ estrogen possible</td>
<td>Monitor menopausal symptoms. The lowest dose of hormonal therapy should be used to achieve menopausal symptom relief.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ medroxyprogesterone possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ micronized progesterone possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ drospirenone possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>See Hormonal Contraceptives for other progestin-NNRTI interactions</td>
<td></td>
</tr>
<tr>
<td><strong>Gender-Affirming Hormone Therapy</strong></td>
<td>EFV, ETR, NVP</td>
<td>↓ estradiol possible</td>
<td>Monitor feminizing effects of estrogen and antiandrogen therapy and adjust dosing as necessary.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↔ goserelin, leuprolide acetate, and spironolactone expected</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ dutasteride and finasteride possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↓ testosterone possible</td>
<td>Monitor masculinizing effects of testosterone and adjust testosterone dose as necessary.</td>
</tr>
<tr>
<td><strong>HMG-CoA Reductase Inhibitors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>EFV, ETR</td>
<td>Atorvastatin AUC ↓ 32%–43%</td>
<td>Adjust atorvastatin according to lipid responses, but do not exceed the maximum recommended dose.</td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>↓ atorvastatin possible</td>
<td>Adjust atorvastatin according to lipid responses, not to exceed the maximum recommended dose.</td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>Atorvastatin AUC ↔</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Atorvastatin metabolites ↑ 23%–39%</td>
<td></td>
</tr>
<tr>
<td>Fluvastatin</td>
<td>EFV, ETR</td>
<td>↑ fluvastatin possible</td>
<td>Dose adjustments for fluvastatin may be necessary. Monitor for fluvastatin toxicity.</td>
</tr>
<tr>
<td>Lovastatin, Simvastatin</td>
<td>EFV</td>
<td>Simvastatin AUC ↓ 68%</td>
<td>Adjust simvastatin dose according to lipid responses, but do not exceed the maximum recommended dose. If EFV is used with a PI/r, simvastatin andLovastatin should be avoided.</td>
</tr>
<tr>
<td></td>
<td>ETR, NVP</td>
<td>↓ lovastatin possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ simvastatin possible</td>
<td>Adjust lovastatin or simvastatin dose according to lipid responses, but do not exceed the maximum recommended dose. If ETR or NVP is used with a PI/r, simvastatin andLovastatin should be avoided.</td>
</tr>
</tbody>
</table>
### Table 18b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs  
*(Last updated October 17, 2017; last reviewed October 17, 2017)*

<table>
<thead>
<tr>
<th>Concomitant Drug Class/ Name</th>
<th>NNRTIa</th>
<th>Effect on NNRTI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HMG-CoA Reductase Inhibitors, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pitavastatin</td>
<td>EFV</td>
<td>Pitavastatin AUC ↓ 11%, $C_{\text{max}}$ ↑ 20%</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td>ETR, NVP, RPV</td>
<td>↔ pitavastatin expected</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>EFV</td>
<td>AUC ↓ 44%</td>
<td>Adjust statin dose according to lipid responses, but do not exceed the maximum recommended dose.</td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>↓ pravastatin possible</td>
<td></td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>EFV, ETR, NVP</td>
<td>↔ rosuvastatin expected</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td><strong>Immunosuppressants</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyclosporine, Everolimus, Sirolimus, Tacrolimus</td>
<td>EFV, ETR, NVP</td>
<td>↓ immunosuppressant possible</td>
<td>Increase in immunosuppressant dose may be necessary. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with specialist as necessary.</td>
</tr>
<tr>
<td><strong>Narcotics/Treatments for Opioid Dependence</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buprenorphine Sublingual or buccal</td>
<td>EFV</td>
<td>Buprenorphine AUC ↓ 50%</td>
<td>No dose adjustment recommended; monitor for withdrawal symptoms.</td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>Buprenorphine AUC ↓ 71%</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>No significant effect</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Buprenorphine Implant</td>
<td>EFV, ETR, NVP</td>
<td>No data</td>
<td>Clinical monitoring is recommended if NNRTI is initiated after insertion of buprenorphine implant.</td>
</tr>
<tr>
<td>Methadone</td>
<td>EFV</td>
<td>Methadone AUC ↓ 52%</td>
<td>Opioid withdrawal common; increased methadone dose often necessary.</td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>No significant effect</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>Methadone AUC ↓ 37% to 51%</td>
<td>Opioid withdrawal common; increased methadone dose often necessary.</td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>R-methadone$^c$ AUC ↓ 16%</td>
<td>No dose adjustment necessary, but monitor for withdrawal symptoms.</td>
</tr>
<tr>
<td><strong>PDE5 Inhibitors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sildenafil</td>
<td>ETR</td>
<td>Sildenafil AUC ↓ 57%</td>
<td>May need to increase sildenafil dose based on clinical effect.</td>
</tr>
<tr>
<td></td>
<td>EFV, NVP</td>
<td>↓ sildenafil possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>↔ sildenafil</td>
<td></td>
</tr>
<tr>
<td>Avanafil, Tadalafil, Vardenafil</td>
<td>EFV, ETR, NVP</td>
<td>↓ PDE5 inhibitor possible</td>
<td>May need to increase PDE5 inhibitor dose based on clinical effect.</td>
</tr>
</tbody>
</table>

*Approved dose for RPV is 25 mg once daily. Most PK interaction studies were performed using 75 to 150 mg per dose.*

*Norbuprenorphine is an active metabolite of buprenorphine.*

*R-methadone is the active form of methadone.*

**Key to Symbols:**

↑ = increase  
↓ = decrease  
↔ = no change

**Key to Acronyms:** ARV = antiretroviral; AUC = area under the curve; BID = twice daily; CCB = calcium channel blockers; $C_{\text{max}}$ = maximum plasma concentration; $C_{\text{min}}$ = minimum plasma concentration; DAA = direct-acting antivirals; DHA = dihydroarteminisin; DMPA = depot medroxyprogesterone acetate; EFV = efavirenz; ETR = etravirine; HMG-CoA = hydroxy-methylglutaryl-coenzyme A; INR = international normalized ratio; MAC = *Mycobacterium avium* complex; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; OH-itraconazole = active metabolite of itraconazole; PCP = *Pneumocystis jiroveci* pneumonia; PDE5 = phosphodiesterase type 5; PI = protease inhibitor; PI/r = protease inhibitor/ritonavir; PK = pharmacokinetic; PPI = proton pump inhibitor; RPV = rilpivirine; RTV = ritonavir

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Downloaded from [https://aidsinfo.nih.gov/guidelines](https://aidsinfo.nih.gov/guidelines) on 8/8/2018
Table 18c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents)  (Last updated October 17, 2017; last reviewed October 17, 2017) (page 1 of 3)

Recommendations for managing a particular drug interaction may differ depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or if a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly.

Note: Interactions associated with didanosine (ddI) and stavudine (d4T) are not included in this table. Please refer to Food and Drug Administration product labels for information regarding interactions between ddI or d4T with other concomitant drugs.

<table>
<thead>
<tr>
<th>Concomitant Drug Class/ Name</th>
<th>NRTI</th>
<th>Effect on NRTI and/or Concomitant Drug Concentrations</th>
<th>Dosage Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cytomegalovirus and Hepatitis B Antivirals</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adefovir</td>
<td>TDF</td>
<td>No data</td>
<td><strong>Do not coadminister.</strong> Serum concentrations of TDF and/or other renally eliminated drugs may be increased.</td>
</tr>
<tr>
<td>Ganciclovir, Valganciclovir</td>
<td>TDF</td>
<td>No data</td>
<td>Serum concentrations of these drugs and/or TDF may increase. Monitor for dose-related toxicities.</td>
</tr>
<tr>
<td>ZDV</td>
<td></td>
<td>No significant effect</td>
<td>Potential increase in hematologic toxicities.</td>
</tr>
<tr>
<td><strong>Hepatitis C Antiviral Agents</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ledipasvir/sofosbuvir, sofosbuvir/velpatasvir, sofosbuvir/velpatasvir/voxilaprevir</td>
<td>TAF, TDF</td>
<td>No significant effect Ledipasvir ↑ TDF AUC 40%–98% when TDF is given with RPV and EFV. Further ↑ TDF possible if TDF is given with PIs.</td>
<td>No dose adjustment. <strong>General recommendations:</strong> The safety of increased TDF exposure when ledipasvir/sofosbuvir is coadministered with TDF and a PI/r, ATV/c, or DRV/c has not been established. Consider alternative HCV or ARV drugs to avoid increased TDF toxicities. Consider using TAF in patients at risk of TDF-associated adverse events. If coadministration with TDF is necessary, monitor for TDF toxicity. Coadministration of ledipasvir/sofosbuvir with EVG/c/TDF/FTC is not recommended.</td>
</tr>
<tr>
<td>Glecaprevir/Pibrentasvir</td>
<td>TAF, TDF</td>
<td>No significant effect</td>
<td>No dose adjustment.</td>
</tr>
<tr>
<td>Ribavirin</td>
<td>ZDV</td>
<td>Ribavirin inhibits phosphorylation of ZDV.</td>
<td>Avoid coadministration if possible, or closely monitor HIV virologic response and possible hematologic toxicities.</td>
</tr>
<tr>
<td><strong>INSTIs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DTG</td>
<td>TAF, TDF</td>
<td>TAF AUC ↔ TDF AUC ↔ DTG AUC ↔</td>
<td>No dose adjustment. No dose adjustment. No dose adjustment.</td>
</tr>
<tr>
<td><strong>Narcotics/Treatment for Opioid Dependence</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>3TC, TDF, TAF, ZDV</td>
<td>No significant effect</td>
<td>No dose adjustment.</td>
</tr>
<tr>
<td>Concomitant Drug Class/ Name</td>
<td>NRTI</td>
<td>Effect on NRTI and/or Concomitant Drug Concentrations</td>
<td>Dosage Recommendations and Clinical Comments</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>------</td>
<td>------------------------------------------------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td><strong>Narcotics/Treatment for Opioid Dependence, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methadone</td>
<td>ABC</td>
<td>Methadone clearance ↑ 22%</td>
<td>No dose adjustment.</td>
</tr>
<tr>
<td></td>
<td>ZDV</td>
<td>ZDV AUC ↑ 29%–43%</td>
<td>Monitor for ZDV-related adverse effects.</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atovaquone</td>
<td>ZDV</td>
<td>ZDV AUC ↑ 31%</td>
<td>Monitor for ZDV-related adverse effects.</td>
</tr>
<tr>
<td><strong>Anticonvulsants</strong></td>
<td>TAF</td>
<td>With carbamazepine: • TAF AUC ↓ 55%</td>
<td>Consider alternative anticonvulsant.</td>
</tr>
<tr>
<td>Carbamazepine, oxcarbazepine, phenobarbital, phenytoin</td>
<td></td>
<td>↓ TAF possible with other anticonvulsants</td>
<td></td>
</tr>
<tr>
<td><strong>Antimycobacterial</strong></td>
<td>TAF</td>
<td>↓ TAF possible</td>
<td>Coadministration is not recommended.</td>
</tr>
<tr>
<td>Rifabutin, rifampin, rifapentine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Herbal Products</strong></td>
<td>TAF</td>
<td>↓ TAF possible</td>
<td>Coadministration is not recommended.</td>
</tr>
<tr>
<td>St. John’s wort</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PIs (HIV)</strong></td>
<td>TAF</td>
<td>TAF 10 mg with ATV/r: • TAF AUC ↑ 91%</td>
<td>No dose adjustment (use TAF 25 mg).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TAF 10 mg with ATV/c: • TAF AUC ↑ 75%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TDF</td>
<td>With ATV (Unboosted): • ATV AUC ↓ 25% and C_{min} ↓ 23% to 40% (higher C_{min} with RTV than without RTV) TDF AUC ↑ 24%–37%</td>
<td>Avoid concomitant use without RTV or COBI. Dose: • ATV 300 mg daily + (RTV 100 mg or COBI 150 mg) daily when coadministered with TDF 300 mg daily. • If using TDF and H2 receptor antagonist in ART-experienced patients, use ATV 400 mg daily + (RTV 100 mg or COBI 150 mg) daily. Monitor for TDF-associated toxicity.</td>
</tr>
<tr>
<td></td>
<td>ZDV</td>
<td>With ATV (Unboosted): • ZDV C_{min} ↓ 30% and AUC ↔</td>
<td>Clinical significance unknown.</td>
</tr>
<tr>
<td><strong>DRV/c</strong></td>
<td>TAF</td>
<td>TAF 25 mg with DRV/c: • TAF ↔</td>
<td>No dose adjustment.</td>
</tr>
<tr>
<td></td>
<td>TDF</td>
<td>↑ TDF possible</td>
<td>Monitor for TDF-associated toxicity.</td>
</tr>
<tr>
<td><strong>DRV/r</strong></td>
<td>TAF</td>
<td>TAF 10 mg with DRV/r: • TAF ↔</td>
<td>No dose adjustment.</td>
</tr>
<tr>
<td></td>
<td>TDF</td>
<td>TDF AUC ↑ 22% and C_{min} ↑ 37%</td>
<td>Clinical significance unknown. Monitor for TDF toxicity.</td>
</tr>
</tbody>
</table>
### Table 18c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents) *(Last updated October 17, 2017; last reviewed October 17, 2017)*  
(page 3 of 3)

<table>
<thead>
<tr>
<th>Concomitant Drug Class/ Name</th>
<th>NRTI</th>
<th>Effect on NRTI and/or Concomitant Drug Concentrations</th>
<th>Dosage Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>PIs (HIV), continued</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LPV/r</td>
<td>TAF 10 mg with DRV/r:</td>
<td>No dose adjustment.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• TAF AUC ↑ 47%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>TDF</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>LPV/r AUC ↓ 15%</td>
<td>Clinical significance unknown. Monitor for TDF toxicity.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TDF AUC ↑ 34%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TPV/r</td>
<td>ABC</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ABC AUC ↓ 35%–44%</td>
<td>Appropriate doses for this combination have not been established.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TAF</td>
<td>Coadministration is not recommended.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TAF expected</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>TDF</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>TPV/r AUC ↓ 9%–18% and C$_{\text{min}}$ ↓ 12%–21%</td>
<td>No dose adjustment.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ZDV</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ZDV AUC ↓ 35%</td>
<td>Appropriate doses for this combination have not been established.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TPV/r AUC ↓ 31%–43%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Key to Symbols:**

↑ = increase  
↓ = decrease  
↔ = no change

**Key to Acronyms:** 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATC/c = atazanavir/cobicistat; AUC = area under the curve; C$_{\min}$ = minimum plasma concentration; COBI, c = cobicistat; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; FTC = emtricitabine; HCV = hepatitis C virus; INSTI = integrase strand transfer inhibitors; LPV/r = lopinavir/ritonavir; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PI/r = ritonavir-boosted protease inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV, r = ritonavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV/r = tipranavir/ritonavir; ZDV = zidovudine
Table 18d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 1 of 11)

This table provides information on known or predicted pharmacokinetic interactions between INSTIs (DTG, EVG, or RAL) and non-ARV drugs. EVG is always coadministered with COBI. Recommendations for managing a particular drug interaction may differ depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or if a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly.

<table>
<thead>
<tr>
<th>Concomitant Drug Class/Name</th>
<th>INSTI</th>
<th>Effect on INSTI or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acid Reducers</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Al, Mg, +/- Ca-Containing Antacids</td>
<td>DTG</td>
<td>DTG AUC ↓ 74% if given simultaneously with antacid</td>
<td>Give DTG at least 2 hours before or at least 6 hours after antacids containing polyvalent cations.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DTG AUC ↓ 26% if given 2 hours before antacid</td>
<td></td>
</tr>
<tr>
<td></td>
<td>EVG/c</td>
<td>EVG AUC ↓ 40%–50% if given simultaneously with antacid</td>
<td>Separate EVG/c/TDF/FTC and antacid administration by more than 2 hours.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EVG AUC ↓ 15%–20% if given 2 hours before or after antacid; ↔ with 4-hour interval</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RAL</td>
<td>Al-Mg Hydroxide Antacid:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>•  RAL C_{\text{min}} ↓ 49% to 63%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>CaCO\textsubscript{3} Antacid:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>•  RAL (400 mg BID) C_{\text{min}} ↓ 32%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>•  RAL (1200 mg once daily) C_{\text{min}} ↓ 48% to 57%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Do not coadminister RAL and Al-Mg hydroxide antacids. Use alternative acid reducing agent.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>With CaCO\textsubscript{3} Antacids:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>•  RAL 1200 mg once daily: Do not coadminister</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>•  RAL 400 mg BID: No dose adjustment or separation necessary</td>
<td></td>
</tr>
<tr>
<td><strong>H2-Receptor Antagonists</strong></td>
<td>EVG/c</td>
<td>No significant effect</td>
<td>No dose adjustment.</td>
</tr>
<tr>
<td><strong>Proton Pump Inhibitors (PPIs)</strong></td>
<td>DTG</td>
<td>No significant effect</td>
<td>No dose adjustment.</td>
</tr>
<tr>
<td></td>
<td>EVG/c</td>
<td>No significant effect</td>
<td>No dose adjustment.</td>
</tr>
<tr>
<td></td>
<td>RAL</td>
<td>RAL AUC ↑ 37% and C_{\text{min}} ↑ 24%</td>
<td>No dose adjustment.</td>
</tr>
<tr>
<td><strong>Anticoagulants and Antiplatelets</strong></td>
<td>Apixaban</td>
<td>EVG/c</td>
<td>↑ apixaban expected</td>
</tr>
<tr>
<td></td>
<td>Betrixaban</td>
<td>EVG/c</td>
<td>↑ betrixaban expected</td>
</tr>
<tr>
<td></td>
<td>Dabigatran</td>
<td>EVG/c</td>
<td>↑ dabigatran expected</td>
</tr>
<tr>
<td></td>
<td>Edoxaban</td>
<td>EVG/c</td>
<td>↑ edoxaban expected</td>
</tr>
<tr>
<td>Concomitant Drug Class/Name</td>
<td>INSTI</td>
<td>Effect on INSTI or Concomitant Drug Concentrations</td>
<td>Dosing Recommendations and Clinical Comments</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>-------</td>
<td>--------------------------------------------------</td>
<td>---------------------------------------------</td>
</tr>
<tr>
<td><strong>Anticoagulants and Antiplatelets, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>EVG/c</td>
<td>↑ rivaroxaban expected</td>
<td><strong>Coadministration is not recommended.</strong> Consider alternative antiretroviral (e.g., an unboosted INSTI) or warfarin.</td>
</tr>
<tr>
<td>Ticagrelor</td>
<td>EVG/c</td>
<td>↑ ticagrelor expected</td>
<td>Avoid concomitant use.</td>
</tr>
<tr>
<td>Vorapaxar</td>
<td>EVG/c</td>
<td>↑ vorapaxar expected</td>
<td>Avoid concomitant use.</td>
</tr>
<tr>
<td>Warfarin</td>
<td>EVG/c</td>
<td>↑ or ↓ warfarin possible</td>
<td>Monitor INR and adjust warfarin dose accordingly.</td>
</tr>
<tr>
<td><strong>Anticonvulsants</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>DTG</td>
<td>DTG AUC ↓ 49%</td>
<td>Increase DTG dose to 50 mg BID in treatment-naive or treatment-experienced, INSTI-naive patients. Use alternative anticonvulsant for INSTI-experienced patients with known or suspected INSTI resistance.</td>
</tr>
<tr>
<td></td>
<td>EVG/c</td>
<td>Carbamazepine AUC ↑ 43%</td>
<td><strong>Contraindicated.</strong></td>
</tr>
<tr>
<td></td>
<td>EVG/c</td>
<td>EVG AUC ↓ 69% and C_min ↓ &gt;99%</td>
<td>↓ COBI expected</td>
</tr>
<tr>
<td></td>
<td>RAL</td>
<td>↓ or ↔ RAL possible</td>
<td><strong>Coadministration is not recommended.</strong></td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>DTG</td>
<td>↓ DTG possible</td>
<td><strong>Coadministration is not recommended.</strong></td>
</tr>
<tr>
<td>Phenytoin</td>
<td>EVG/c</td>
<td>↓ EVG/c expected</td>
<td><strong>Contraindicated.</strong></td>
</tr>
<tr>
<td></td>
<td>RAL</td>
<td>↓ or ↔ RAL possible</td>
<td><strong>Coadministration is not recommended.</strong></td>
</tr>
<tr>
<td>Ethosuximide</td>
<td>EVG/c</td>
<td>↑ ethosuximide possible</td>
<td>Clinically monitor for ethosuximide toxicities.</td>
</tr>
<tr>
<td>Oxcarbazepine</td>
<td>DTG, EVG/c</td>
<td>↓ INSTI possible</td>
<td>Consider alternative anticonvulsant.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ cobicistat possible</td>
<td></td>
</tr>
<tr>
<td><strong>Antidepressants/Anxiolytics/Antipsychotics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bupropion</td>
<td>EVG/c</td>
<td>↑ or ↓ bupropion possible</td>
<td>Titrate bupropion dose based on clinical response.</td>
</tr>
<tr>
<td>Buspirone</td>
<td>EVG/c</td>
<td>↑ buspirone possible</td>
<td>Initiate buspirone at a low dose. Dose reduction may be necessary.</td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>EVG/c</td>
<td>↑ or ↓ EVG possible</td>
<td>Consider alternative antidepressant or ARV.</td>
</tr>
<tr>
<td>Lurasidone</td>
<td>EVG/c</td>
<td>↑ lurasidone expected</td>
<td><strong>Contraindicated.</strong></td>
</tr>
<tr>
<td>Pimozide</td>
<td>EVG/c</td>
<td>↑ pimozide expected</td>
<td><strong>Contraindicated.</strong></td>
</tr>
<tr>
<td>Quetiapine</td>
<td>EVG/c</td>
<td>↑ quetiapine AUC expected</td>
<td><strong>Initiation of Quetiapine in a Patient Receiving EVG/c:</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Start quetiapine at the lowest dose and titrate up as needed. Monitor for quetiapine efficacy and adverse effects.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Initiation of EVG/c in a Patient Receiving a Stable Dose of Quetiapine:</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Reduce quetiapine dose to 1/6 of the original dose, and closely monitor for quetiapine efficacy and adverse effects.</td>
</tr>
</tbody>
</table>
Table 18d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs  *(Last updated October 17, 2017; last reviewed October 17, 2017)*  (page 3 of 11)

<table>
<thead>
<tr>
<th>Concomitant Drug Class/Name</th>
<th>INSTI</th>
<th>Effect on INSTI or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antidepressants/Anxiolytics/Antipsychotics Also see Sedative/Hypnotics section below.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Selective Serotonin Reuptake Inhibitors (SSRIs)</td>
<td>EVG/c</td>
<td>↔ EVG &amp; ↔ sertraline</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ other SSRI possible</td>
<td></td>
</tr>
<tr>
<td>Citalopram, escitalopram, fluoxetine, paroxetine, sertraline</td>
<td>RAL</td>
<td>↔ RAL</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>↔ citalopram</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>↔ SSRI expected</td>
<td></td>
</tr>
<tr>
<td></td>
<td>DTG</td>
<td>↔ DTG</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↔ citalopram</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>↔ SSRI expected</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tricyclic Antidepressants (TCAs)</td>
<td>EVG/c</td>
<td>Desipramine AUC ↑ 65%</td>
<td>Initiate with lowest dose of TCA and titrate dose carefully.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ TCA expected</td>
<td></td>
</tr>
<tr>
<td>Amitriptyline, desipramine, doxepin, imipramine, nortriptyline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trazodone</td>
<td>EVG/c</td>
<td>↑ trazodone possible</td>
<td>Initiate with lowest dose of trazadone and titrate dose carefully.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antifungals</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isavuconazole</td>
<td>EVG/c</td>
<td>↑ isavuconazole expected</td>
<td>If coadministered, consider monitoring isavuconazole concentrations and assess virologic response.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ EVG and COBI possible</td>
<td></td>
</tr>
<tr>
<td>Itraconazole</td>
<td>EVG/c</td>
<td>↑ itraconazole expected</td>
<td>Consider monitoring itraconazole level to guide dosage adjustments. High itraconazole doses (&gt;200 mg/day) are not recommended unless dose is guided by itraconazole levels.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ EVG and COBI possible</td>
<td></td>
</tr>
<tr>
<td>Posaconazole</td>
<td>EVG/c</td>
<td>↑ EVG and COBI possible</td>
<td>If coadministered, monitor posaconazole concentrations.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ posaconazole possible</td>
<td></td>
</tr>
<tr>
<td>Voriconazole</td>
<td>EVG/c</td>
<td>↑ voriconazole expected</td>
<td>Risk/benefit ratio should be assessed to justify use of voriconazole. If administered, consider monitoring voriconazole level. Adjust dose accordingly.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ EVG and COBI possible</td>
<td></td>
</tr>
<tr>
<td>Antihyperglycemics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saxagliptin</td>
<td>EVG/c</td>
<td>↑ saxagliptin expected</td>
<td>Limit saxagliptin dose to 2.5 mg once daily.</td>
</tr>
<tr>
<td>Dapagliflozin/Saxagliptin</td>
<td>EVG/c</td>
<td>↑ saxagliptin expected</td>
<td>Do not coadminister, as this coformulated drug contains 5 mg of saxagliptin.</td>
</tr>
<tr>
<td>Antimycobacterials</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>EVG/c</td>
<td>↑ clarithromycin possible</td>
<td>CrCl 50–60 mL/min:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ COBI possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Reduce clarithromycin dose by 50%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CrCl &lt;50 mL/min:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• EVG/c is not recommended</td>
<td></td>
</tr>
</tbody>
</table>
### Antimycobacterials, continued

<table>
<thead>
<tr>
<th>Concomitant Drug Class/Name</th>
<th>INSTI</th>
<th>Effect on INSTI or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rifabutin</strong></td>
<td>DTG</td>
<td>Rifabutin (300 mg Once Daily):</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• DTG AUC ↔ and C&lt;sub&gt;min&lt;/sub&gt; ↓ 30%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>EVG/c</td>
<td>Rifabutin 150 mg Every Other Day with EVG/c Once Daily Compared to Rifabutin 300 mg Once Daily Alone:</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• ↔ rifabutin AUC</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 25-O-desacetyl-rifabutin AUC ↑ 625%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RAL</td>
<td>RAL AUC ↑ 19%, C&lt;sub&gt;min&lt;/sub&gt; ↓ 20%</td>
<td></td>
</tr>
<tr>
<td><strong>Rifampin</strong></td>
<td>DTG</td>
<td>Rifampin with DTG 50 mg BID Compared to DTG 50 mg BID Alone:</td>
<td>Dose:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• DTG AUC ↓ 54%, C&lt;sub&gt;min&lt;/sub&gt; ↓ 72%</td>
<td>• DTG 50 mg BID (instead of 50 mg once daily) for patients without suspected or documented INSTI mutation.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rifampin with DTG 50 mg BID Compared to DTG 50 mg Once Daily Alone:</td>
<td>Alternative to rifampin should be used in patients with certain suspected or documented INSTI-associated resistance substitutions. Consider using rifabutin.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• DTG AUC ↑ 33%, C&lt;sub&gt;min&lt;/sub&gt; ↑ 22%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>EVG/c</td>
<td>Significant ↓ EVG and COBI expected</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td></td>
<td>RAL</td>
<td>RAL 400 mg:</td>
<td>Dose:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• RAL AUC ↓ 40%, C&lt;sub&gt;min&lt;/sub&gt; ↓ 61%</td>
<td>• RAL 800 mg BID, instead of 400 mg BID</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rifampin with RAL 800 mg BID Compared to RAL 400 mg BID Alone:</td>
<td>Do not coadminister RAL 1200 mg once daily with rifampin.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• RAL AUC ↑ 27%, C&lt;sub&gt;min&lt;/sub&gt; ↓ 53%</td>
<td>Monitor closely for virologic response or consider using rifabutin as an alternative rifamycin.</td>
</tr>
<tr>
<td><strong>Rifapentine</strong></td>
<td>DTG</td>
<td>Significant ↓ DTG expected</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td>EVG/c</td>
<td>Significant ↓ EVG and COBI expected</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td>RAL</td>
<td>Rifapentine 900 mg Once Weekly:</td>
<td>For once-weekly rifapentine, use standard RAL 400 mg BID doses.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• RAL AUC ↑ 71%, C&lt;sub&gt;min&lt;/sub&gt; ↓ 12%</td>
<td>Do not coadminister with once-daily rifapentine.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rifapentine 600 mg Once Daily:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• RAL C&lt;sub&gt;min&lt;/sub&gt; ↓ 41%</td>
<td></td>
</tr>
</tbody>
</table>

### Cardiac Medications

**Antiarrhythmics**

- Amiodarone, bepridil, digoxin, disopyramide, dronedarone, flecainide, systemic lidocaine, mexiletine, propafenone, quinidine

<table>
<thead>
<tr>
<th>INSTI</th>
<th>Effect on INSTI or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVG/c</td>
<td>† antiarrhythmics possible</td>
<td>Use antiarrhythmics with caution. Therapeutic drug monitoring, if available, is recommended for antiarrhythmics.</td>
</tr>
<tr>
<td></td>
<td>Digoxin C&lt;sub&gt;max&lt;/sub&gt; ↑ 41% and no significant change in AUC</td>
<td></td>
</tr>
<tr>
<td>Concomitant Drug Class/Name</td>
<td>INSTI</td>
<td>Effect on INSTI or Concomitant Drug Concentrations</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>-------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td><strong>Cardiac Medications</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bosentan</td>
<td>EVG/c</td>
<td>↑ bosentan possible</td>
</tr>
<tr>
<td></td>
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<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beta-blockers (e.g., metoprolol, timolol)</td>
<td>EVG/c</td>
<td>↑ beta-blockers possible</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium Channel Blockers (CCBs)</td>
<td>EVG/c</td>
<td>↑ CCBs possible</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dofetilide</td>
<td>DTG</td>
<td>↑ dofetilide expected</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eplerenone</td>
<td>EVG/c</td>
<td>↑ eplerenone expected</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ranolazine</td>
<td>EVG/c</td>
<td>↑ ranolazine expected</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ivabradine</td>
<td>EVG/c</td>
<td>↑ ivabradine expected</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Corticosteroids</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beclomethasone Inhaled or intranasal</td>
<td>EVG/c</td>
<td>↔ expected</td>
</tr>
<tr>
<td>Budesonide, Ciclesonide, Fluticasone, Mometasone Inhaled or intranasal</td>
<td>EVG/c</td>
<td>↑ glucocorticoid possible</td>
</tr>
<tr>
<td>Betamethasone, Budesonide Systemic</td>
<td>EVG/c</td>
<td>↑ glucocorticoids possible</td>
</tr>
<tr>
<td>Dexamethasone Systemic</td>
<td>EVG/c</td>
<td>↓ EVG and COBI possible</td>
</tr>
<tr>
<td>Prednisone, Prednisolone Systemic</td>
<td>EVG/c</td>
<td>↑ prednisolone possible</td>
</tr>
<tr>
<td>Concomitant Drug Class/Name</td>
<td>INSTI</td>
<td>Effect on INSTI or Concomitant Drug Concentrations</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>-------</td>
<td>---------------------------------------------------</td>
</tr>
<tr>
<td><strong>Corticosteroids, continued</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Betamethasone, Methylprednisolone, Prednisolone, Triamcinolone</td>
<td>EVG/c</td>
<td>↑ glucocorticoids expected</td>
</tr>
<tr>
<td>Local injections, including intra-articular, epidural, or intra-orbital</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hepatitis C Direct Acting Antivirals</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daclatasvir</td>
<td>DTG</td>
<td>↔ daclatasvir</td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ daclatasvir</td>
<td>Decrease daclastavir dose to 30 mg once daily.</td>
</tr>
<tr>
<td>RAL</td>
<td>No data</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td>Dasabuvir + Ombitasvir/Paritaprevir</td>
<td>DTG</td>
<td>No data</td>
</tr>
<tr>
<td>EVG/c</td>
<td>No data</td>
<td></td>
</tr>
<tr>
<td>RAL</td>
<td>RAL AUC ↑ 134%</td>
<td></td>
</tr>
<tr>
<td>Elbasvir/Grazoprevir</td>
<td>DTG</td>
<td>↔ elbasvir</td>
</tr>
<tr>
<td></td>
<td>↔ grazoprevir</td>
<td></td>
</tr>
<tr>
<td></td>
<td>↔ DTG</td>
<td></td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ elbasvir, grazoprevir expected</td>
<td><strong>Coadministration is not recommended.</strong></td>
</tr>
<tr>
<td>RAL</td>
<td>↔ elbasvir</td>
<td></td>
</tr>
<tr>
<td></td>
<td>↔ grazoprevir</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RAL ↔ with elbasvir</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RAL AUC ↑ 43% with grazoprevir</td>
<td></td>
</tr>
<tr>
<td>Glecaprevir/Pibrentasvir</td>
<td>DTG, RAL</td>
<td>No significant effect</td>
</tr>
<tr>
<td>EVG/c</td>
<td>Glecaprevir AUC ↑ 3-fold</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pibrentasvir AUC ↑ 57%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>EVG AUC ↑ 47%</td>
<td></td>
</tr>
<tr>
<td>Ledipasvir/Sofosbuvir</td>
<td>EVG/c/TDF/FTC</td>
<td>↑ TDF and ↑ ledipasvir expected</td>
</tr>
<tr>
<td></td>
<td>↔ EVG/c/TAF/FTC expected</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td>DTG, RAL</td>
<td>↔ DTG or RAL</td>
</tr>
<tr>
<td>Simeprevir</td>
<td>DTG</td>
<td>↔ expected</td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ simeprevir expected</td>
<td><strong>Coadministration is not recommended.</strong></td>
</tr>
<tr>
<td>RAL</td>
<td>↔ expected</td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir</td>
<td>All INSTIs</td>
<td>↔ expected</td>
</tr>
<tr>
<td>Sofosbuvir/Velpatasvir</td>
<td>All INSTIs</td>
<td>↔ expected</td>
</tr>
</tbody>
</table>
### Table 18d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 7 of 11)

<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>Hepatitis C Direct Acting Antivirals, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Sofosbuvir/ Velpatasvir/ Voxilaprevir | EVG/c | When Given with Sofosbuvir/Velpatasvir/ Voxilaprevir (400/100/100 mg) + Voxilaprevir 100 mg:  
- Sofosbuvir AUC ↑ 22%  
- ↔ velpatasvir  
- Voxilaprevir AUC ↑ 2-fold | No dose adjustment necessary. |
| DTG, RAL | ↔ expected | | No dose adjustment necessary. |
| **Herbal Products** | | | |
| St. John's Wort | DTG | ↓ DTG possible | Do not coadminister. |
| EVG/c | ↓ EVG and COBI possible | Contraindicated. |
| **Hormonal Therapies** | | | |
| **Hormonal Contraceptives** | DTG, RAL | ↔ ethinyl estradiol, norgestimate, and DTG or RAL | No dose adjustment necessary. |
| EVG/c | Norgestimate AUC, C<sub>max</sub>, and C<sub>min</sub> ↑ >2-fold  
Ethinyl estradiol AUC ↓ 25% and C<sub>min</sub> ↓ 44% | The effects of increases in progestin (norgestimate) are not fully known and can include insulin resistance, dyslipidemia, acne, and venous thrombosis. Weigh the risks and benefits of the drug, and consider alternative contraceptive method. |
| † drospirenone possible | Clinical monitoring is recommended, due to the potential for hyperkalemia. |
| **Menopausal Hormone Replacement Therapy** | DTG, RAL | With estradiol or conjugated estrogen (equine and synthetic): ↓ estrogen possible  
 ↔ drospirenone, medroxyprogesterone, or micronized progesterone expected | No dose adjustment necessary. |
| EVG/c | ↓ estrogen possible  
 † drospirenone possible  
 † oral medroxyprogesterone possible  
 † oral micronized progesterone possible | Adjust estrogen and progestin dose as needed based on clinical effects. |
| **Gender-Affirming Hormone Therapy** | DTG, RAL | ↔ estrogen expected | No dose adjustment necessary. |
| DTG, EVG/c, RAL | ↔ finasteride, goserelin, leuprolide acetate, spironolactone expected | | |
| EVG/c | ↓ estradiol possible  
 † dutasteride possible | Adjust dutasteride dosage as needed based on clinical effects and endogenous hormone concentrations. |
| EVG/c | ↑ testosterone possible | Monitor masculinizing effects of testosterone and for adverse effects and adjust testosterone dose as necessary. |
| DTG, RAL | ↔ testosterone expected | No dose adjustment necessary. |
### Table 18d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 8 of 11)

<table>
<thead>
<tr>
<th>Concomitant Drug Class/Name</th>
<th>INSTI</th>
<th>Effect on INSTI or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HMG-CoA Reductase Inhibitors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>EVG/c</td>
<td>↑ atorvastatin AUC 2.6-fold and C&lt;sub&gt;max&lt;/sub&gt; 2.3-fold</td>
<td>Titrate statin dose carefully and use the lowest dose necessary while monitoring for toxicities. Do not exceed 20 mg atorvastatin daily.</td>
</tr>
<tr>
<td>Lovastatin</td>
<td>EVG/c</td>
<td>Significant ↑ lovastatin expected</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td>Pitavastatin, Pravastatin</td>
<td>EVG/c</td>
<td>No data</td>
<td>No dosage recommendation</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>EVG/c</td>
<td>Rosuvastatin AUC ↑ 38% and C&lt;sub&gt;max&lt;/sub&gt; ↑ 89%</td>
<td>Titrate statin dose carefully and use the lowest dose necessary while monitoring for toxicities.</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>EVG/c</td>
<td>Significant ↑ simvastatin expected</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td><strong>Immunosuppressants</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyclosporine, Everolimus, Sirolimus, Tacrolimus</td>
<td>EVG/c</td>
<td>↑ immunosuppressant possible</td>
<td>Initiate with an adjusted immunosuppressant dose to account for potential increased concentration and monitor for toxicities. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with specialist as necessary.</td>
</tr>
<tr>
<td><strong>Narcotics/Treatment for Opioid Dependence</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buprenorphine Sublingual, buccal, or implant</td>
<td>EVG/c</td>
<td>Buprenorphine AUC ↑ 35%, C&lt;sub&gt;max&lt;/sub&gt; ↑ 12%, and C&lt;sub&gt;min&lt;/sub&gt; ↑ 66% Norbuprenorphine AUC ↑ 42%, C&lt;sub&gt;max&lt;/sub&gt; ↑ 24%, and C&lt;sub&gt;min&lt;/sub&gt; ↑ 57%</td>
<td>No dose adjustment necessary. Clinical monitoring is recommended. When transferring buprenorphine from transmucosal to implantation, monitor to ensure buprenorphine effect is adequate and not excessive.</td>
</tr>
<tr>
<td>Methadone</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAL</td>
<td>EVG/c</td>
<td>No significant effect</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td>RAL</td>
<td>No significant effect</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td>RAL</td>
<td>No significant effect</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td><strong>Neuroleptics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perphenazine, Risperidone, Thioridazine</td>
<td>EVG/c</td>
<td>↑ neuroleptic possible</td>
<td>Initiate neuroleptic at a low dose. Decrease in neuroleptic dose may be necessary.</td>
</tr>
<tr>
<td><strong>PDE5 Inhibitors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avanafil</td>
<td>EVG/c</td>
<td>No data</td>
<td>Coadministration is not recommended.</td>
</tr>
<tr>
<td>Sildenafil</td>
<td>EVG/c</td>
<td>↑ sildenafil expected</td>
<td>For Treatment of Erectile Dysfunction:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Start with sildenafil 25 mg every 48 hours and monitor for adverse effects of sildenafil.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>For treatment of PAH:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Contraindicated.</td>
</tr>
</tbody>
</table>
### Table 18d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 9 of 11)

<table>
<thead>
<tr>
<th>Concomitant Drug Class/Name</th>
<th>INSTI</th>
<th>Effect on INSTI or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PDE5 Inhibitors, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tadalafil</td>
<td>EVG/c</td>
<td>↑ tadalafil expected</td>
<td>For Treatment of Erectile Dysfunction:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Start with tadalafil 5-mg dose and do not</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>exceed a single dose of 10 mg every 72 hours.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Monitor for adverse effects of tadalafil.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>For Treatment of PAH:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>In patients on EVG/c &gt;7 days:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Start with tadalafil 20 mg once daily and</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>increase to 40 mg once daily based on</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>tolerability.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>In patients on tadalafil who require EVG/c:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Stop tadalafil ≥24 hours before EVG/c</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>initiation. Restart tadalafil at 20 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>once daily, and increase to 40 mg once</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>daily based on tolerability.</td>
</tr>
<tr>
<td>Vardenafil</td>
<td>EVG/c</td>
<td>↑ vardenafil expected</td>
<td>Start with vardenafil 2.5 mg every 72 hours</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>and monitor for adverse effects of</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>vardenafil.</td>
</tr>
<tr>
<td><strong>Sedative/Hypnotics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clonazepam, Clorazepate,</td>
<td>EVG/c</td>
<td>↑ benzodiazepines possible</td>
<td>Dose reduction of benzodiazepine may be</td>
</tr>
<tr>
<td>Diazepam, Estazolam,</td>
<td></td>
<td></td>
<td>necessary. Initiate with low dose and</td>
</tr>
<tr>
<td>Flurazepam</td>
<td></td>
<td></td>
<td>clinically monitor.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Consider alternative benzodiazepines to</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>diazepam, such as lorazepam, oxazepam, or</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>temazepam.</td>
</tr>
<tr>
<td>Midazolam, Triazolam</td>
<td>DTG</td>
<td>With DTG 25 mg:</td>
<td>No dose adjustment necessary.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• midazolam AUC ↔</td>
<td></td>
</tr>
<tr>
<td></td>
<td>EVG/c</td>
<td>↑ midazolam expected</td>
<td>Contraindicated. Do not coadminister</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ triazolam expected</td>
<td>triazolam or oral midazolam and EVG/c.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Parenteral midazolam can be used with</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>caution in a closely monitored setting.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Consider dose reduction, especially if</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>more than one dose is administered.</td>
</tr>
<tr>
<td>Suvorexant</td>
<td>EVG/c</td>
<td>↑ suvorexant expected</td>
<td>Coadministration is not recommended.</td>
</tr>
<tr>
<td>Zolpidem</td>
<td>EVG/c</td>
<td>↑ zolpidem expected</td>
<td>Initiate zolpidem at a low dose. Dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>reduction may be necessary.</td>
</tr>
<tr>
<td><strong>Miscellaneous Drugs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alfuzosin</td>
<td>EVG/c</td>
<td>↑ alfuzosin expected</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td>Calcifediol</td>
<td>EVG/c</td>
<td>↑ calcifediol possible</td>
<td>Dose adjustment of calcifediol may be</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>required, and serum 25-hydroxyvitamin D,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>intact PTH, and serum Ca concentrations</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>should be closely monitored.</td>
</tr>
<tr>
<td>Cisapride</td>
<td>EVG/c</td>
<td>↑ cisapride expected</td>
<td>Contraindicated.</td>
</tr>
</tbody>
</table>
### Table 18d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017)  (page 10 of 11)

<table>
<thead>
<tr>
<th>Concomitant Drug Class/Name</th>
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<th>Effect on INSTI or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Miscellaneous Drugs, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Colchicine                  | EVG/c | ↑ colchicine expected                             | Do not coadminister in patients with hepatic or renal impairment.  
  For Treatment of Gout Flares:  
  • Colchicine 0.6 mg for 1 dose, followed by 0.3 mg 1 hour later. Do not repeat dose for at least 3 days.  
  For Prophylaxis of Gout Flares:  
  • If original dose was colchicine 0.6 mg BID, decrease to colchicine 0.3 mg once daily. If regimen was 0.6 mg once daily, decrease to 0.3 mg every other day.  
  For Treatment of Familial Mediterranean Fever:  
  • Do not exceed colchicine 0.6 mg once daily or 0.3 mg BID. |
| Ergot Derivatives           | EVG/c | ↑ dihydroergotamine, ergotamine, methylergonovine expected | Contraindicated. |
| Dronabinol                  | EVG/c | ↑ dronabinol possible                              | Monitor for dronabinol-related adverse effects. |
| Eluxadoline                 | EVG/c | ↑ eluxadoline possible                             | Monitor for eluxadoline-related adverse effects. |
| Flibanserin                 | EVG/c | ↑ flibanserin expected                             | Contraindicated. |
| Metformin                   | DTG   | DTG 50 mg Once Daily + Metformin 500 mg BID:  
  • Metformin AUC ↑ 79%, C_{max} ↑ 66%  
  DTG 50 mg BID + Metformin 500 mg BID:  
  • Metformin AUC ↑ 2.4-fold, C_{max} ↑ 2-fold | Start metformin at lowest dose and titrate based on glycemic control. Monitor for metformin adverse effects.  
  When starting/stopping DTG in patients on metformin, dose adjustment of metformin may be necessary to maintain optimal glycemic control and/or minimize adverse effects of metformin. |
| Polyvalent Cation Supplements | All INSTIs | ↓ INSTI possible  
  DTG ↔ when administered with Ca or Fe supplement simultaneously with food | If coadministration is necessary, give INSTI at least 2 hours before or at least 6 hours after supplements containing polyvalent cations, including but not limited to the following products: cation-containing laxatives; Fe, Ca, or Mg supplements; and sucralfate. Monitor for virologic efficacy.  
  DTG and supplements containing Ca or Fe can be taken simultaneously with food.  
  Many oral multivitamins also contain varying amounts of polyvalent cations; the extent and significance of chelation is unknown. |
| Salmeterol                  | EVG/c | ↑ salmeterol possible                              | Do not coadminister, due to potential increased risk of salmeterol-associated cardiovascular events. |

*Note: Please refer to the Acid Reducers section in this table for recommendations on use with Al-, Mg-, and Ca-containing antacids.*
Table 18d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 11 of 11)

**Key to Acronyms:** Al = aluminum; ART = antiretroviral therapy; ARV = antiretroviral; AUC = area under the curve; BID = twice daily; Ca = calcium; CaCO$_3$ = calcium carbonate; CCB = calcium channel blocker; $C_{\text{max}}$ = maximum plasma concentration; $C_{\text{min}}$ = minimum plasma concentration; COBI, c = cobicistat; CrCl = creatinine clearance; CYP = cytochrome P; DTG = dolutegravir; EVG = elvitegravir; Fe = iron; FTC = emtricitabine; GI = gastrointestinal; INR = international normalized ratio; INSTI = integrase strand transfer inhibitor; Mg = magnesium; PAH = pulmonary arterial hypertension; PI = protease inhibitor; PI/r = ritonavir-boosted protease inhibitor; PPI = proton pump inhibitor; PTH = parathyroid hormone; r = ritonavir; RAL = raltegravir; TDF = tenofovir disoproxil fumarate; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant; Zn = zinc
Table 18e. Drug Interactions between CCR5 Antagonist (Maraviroc) and Other Drugs (Including Antiretroviral Agents)  
(last updated October 17, 2017; last reviewed October 17, 2017) (page 1 of 3)

In the table below, “no dosage adjustment” indicates that the Food and Drug Administration-approved dose of MVC 300 mg twice daily should be used. Recommendations for managing a particular drug interaction may differ depending on whether a new ARV is being initiated in a patient on a stable concomitant medication, or if a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly.

<table>
<thead>
<tr>
<th>Concomitant Drug Class/Name</th>
<th>CCR5 Antagonist</th>
<th>Effect on CCR5 Antagonist and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anticonvulsants</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbamazepine, Phenobarbital, Phenytoin</td>
<td>MVC</td>
<td>↓ MVC possible</td>
<td>If used without a strong CYP3A inhibitor, use MVC 600 mg BID or an alternative antiepileptic agent.</td>
</tr>
<tr>
<td><strong>Antifungals</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isavuconazole</td>
<td>MVC</td>
<td>↑ MVC possible</td>
<td>Consider dose reduction to MVC 150 mg BID.</td>
</tr>
</tbody>
</table>
| Itraconazole                | MVC | ↑ MVC possible | Dose:  
  - MVC 150 mg BID |
| Posaconazole                | MVC | ↑ MVC possible | Dose:  
  - MVC 150 mg BID |
| Voriconazole                | MVC | ↑ MVC possible | Consider dose reduction to MVC 150 mg BID. |
| **Antimycobacterials**      |                |                                               |                                               |
| Clarithromycin              | MVC | ↑ MVC possible | Dose:  
  - MVC 150 mg BID |
| Rifabutin                   | MVC | ↓ MVC possible | If used without a strong CYP3A inducer or inhibitor, no dosage adjustment.  
  If used with a strong CYP3A inhibitor, use MVC 150 mg BID. |
| Rifampin                    | MVC | MVC AUC ↓ 64% | Dose:  
  - MVC 600 mg BID |
| Rifapentine                 | MVC | ↓ MVC expected | Do not coadminister. |
| **Hepatitis C Direct-Acting Antivirals** | | | |
| Daclatasvir                  | MVC | ↔ MVC expected | No dosage adjustment.  
  ↔ Daclatasvir expected |
| Dasabuvir + Ombitasvir/Paritaprevir/RTV | MVC | ↑ MVC expected | Do not coadminister. |
| Elbasvir/Grazoprevir         | MVC | No data | No dosing recommendations at this time. |
| Ledipasvir/Sofosbuvir        | MVC | ↔ MVC expected | No dosage adjustment. |
| Glecaprevir/Pibrentasvir     | MVC | ↔ MVC expected | No dosage adjustment. |
| Simeprevir                   | MVC | ↔ MVC expected | No dosage adjustment. |
| Sofosbuvir                   | MVC | ↔ MVC expected | No dosage adjustment. |
| Sofosbuvir/Velpatasvir       | MVC | ↔ MVC expected | No dosage adjustment. |
### Table 18e. Drug Interactions between CCR5 Antagonist (Maraviroc) and Other Drugs (Including Antiretroviral Agents)  
(Last updated October 17, 2017; last reviewed October 17, 2017)  
(page 2 of 3)

<table>
<thead>
<tr>
<th>Concomitant Drug Class/ Name</th>
<th>CCR5 Antagonist</th>
<th>Effect on CCR5 Antagonist and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hepatitis C Direct-Acting Antivirals, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir/Velpatasvir/ Voxilaprevir</td>
<td>MVC</td>
<td>↔ MVC expected</td>
<td>No dosage adjustment.</td>
</tr>
<tr>
<td><strong>Herbal Products</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>St. John’s Wort</td>
<td>MVC</td>
<td>↓ MVC expected</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
<tr>
<td><strong>Hormonal Therapies</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hormonal Contraceptives</td>
<td>MVC</td>
<td>Ethinyl estradiol or levonorgestrel</td>
<td>No dosage adjustment.</td>
</tr>
<tr>
<td>Menopausal Hormone Replacement Therapy</td>
<td>MVC</td>
<td>↔ MVC or hormone replacement therapies expected</td>
<td>No dosage adjustment.</td>
</tr>
<tr>
<td>Gender-Affirming Hormone Therapies</td>
<td>MVC</td>
<td>↔ MVC or gender-affirming hormones expected</td>
<td>No dosage adjustment.</td>
</tr>
<tr>
<td><strong>ARV Drugs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>INSTIs</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| EVG/c | MVC | ↑ MVC possible | **Dose:**  
• MVC 150 mg BID |
| RAL | MVC | MVC AUC ↓ 21%  
RAL AUC ↓ 37% | No dosage adjustment. |
| NNRTIs | | | |
| EFV | MVC | MVC AUC ↓ 45% | **Dose:**  
• MVC 600 mg BID |
| ETR | MVC | MVC AUC ↓ 53% | **Dose:**  
• MVC 600 mg BID in the absence of a potent CYP3A inhibitor |
| NVP | MVC | MVC AUC ↔ | Without HIV PI:  
• MVC 300 mg BID  
With HIV PI (except TPV/r):  
• MVC 150 mg BID |
| **PIs** | | | |
| ATV +/- RTV or COBI | MVC | With Unboosted ATV:  
• MVC AUC ↑ 257%  
With (ATV 300 mg + RTV 100 mg) Once Daily:  
• MVC AUC ↑ 388% | **Dose:**  
• MVC 150 mg BID |
Table 18e. Drug Interactions between CCR5 Antagonist (Maraviroc) and Other Drugs (Including Antiretroviral Agents) *(Last updated October 17, 2017; last reviewed October 17, 2017)* (page 3 of 3)

<table>
<thead>
<tr>
<th>Concomitant Drug Class/ Name</th>
<th>CCR5 Antagonist</th>
<th>Effect on CCR5 Antagonist and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PIs, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>DRV/c</strong> or <strong>DRV/r</strong></td>
<td>MVC</td>
<td>With (DRV 600 mg + RTV 100 mg) BID:</td>
<td>Dose:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• MVC AUC ↑ 305%</td>
<td>• MVC 150 mg BID</td>
</tr>
<tr>
<td></td>
<td></td>
<td>With (DRV 600 mg + RTV 100 mg) BID and ETR:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• MVC AUC ↑ 210%</td>
<td></td>
</tr>
<tr>
<td><strong>LPV/r</strong></td>
<td>MVC</td>
<td>MVC AUC ↑ 295%</td>
<td>Dose:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>With LPV/r and EFV:</td>
<td>• MVC 150 mg BID</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• MVC AUC ↑ 153%</td>
<td></td>
</tr>
<tr>
<td><strong>RTV</strong></td>
<td>MVC</td>
<td>With RTV 100 mg, BID:</td>
<td>Dose:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• MVC AUC ↑ 161%</td>
<td>• MVC 150 mg BID</td>
</tr>
<tr>
<td><strong>TPV/r</strong></td>
<td>MVC</td>
<td>With (TPV 500 mg + RTV 200 mg) BID:</td>
<td>No dosage adjustment.</td>
</tr>
</tbody>
</table>

**Key to Symbols:**
- ↑ = increase
- ↓ = decrease
- ↔ = no change

**Key to Acronyms:** ARV = antiretroviral; ATV = atazanavir; AUC = area under the curve; BID = twice daily; COBI = cobicistat; CYP = cytochrome P; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; INSTI = integrase strand transfer inhibitor; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; RAL = raltegravir; RTV = ritonavir; TPV = tipranavir; TPV/r = tipranavir/ritonavir
Table 19a. Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors\(^a\) (Last updated October 17, 2017; last reviewed October 17, 2017)  (Page 1 of 2)

**Note:** Delavirdine (DLV), fosamprenavir (FPV), indinavir (IDV), nelfinavir (NFV), and saquinavir (SQV) are not included in this table. Please refer to the Food and Drug Administration product labels for DLV, FPV, IDV, NFV, and SQV for information regarding drug interactions.

<table>
<thead>
<tr>
<th>Pls</th>
<th>PK Data</th>
<th>EFV</th>
<th>ETR</th>
<th>NVP</th>
<th>RPV(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATV Unboosted</td>
<td></td>
<td>EFV: No significant change</td>
<td>ETR AUC ↑ 50% and (C_{\text{min}}) ↑ 58%</td>
<td>↓ ATV possible</td>
<td>↑ RPV possible</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ATV AUC ↓ 74%</td>
<td>ATV AUC ↓ 17% and (C_{\text{min}}) ↓ 47%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose</td>
<td>Do not coadminister.</td>
<td>Do not coadminister.</td>
<td>Do not coadminister.</td>
<td>Standard doses</td>
<td></td>
</tr>
<tr>
<td>ATV/c</td>
<td>PK Data</td>
<td>↓ ATV possible</td>
<td>↓ ATV possible</td>
<td>↓ ATV possible</td>
<td>↑ RPV possible</td>
</tr>
<tr>
<td>Dose</td>
<td>EFV standard dose</td>
<td>↓ COBI possible</td>
<td>↓ COBI possible</td>
<td>↓ COBI possible</td>
<td>↔ ATV expected</td>
</tr>
<tr>
<td>In ART-Naive Patients:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• ATV 400 mg + COBI 150 mg once daily</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Do not use coformulated ATV/c 300 mg/150 mg.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In ART-Experienced Patients:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Do not coadminister.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATV/r</td>
<td>PK Data</td>
<td></td>
<td></td>
<td></td>
<td>↑ RPV possible</td>
</tr>
<tr>
<td>Once Daily:</td>
<td>(ATV 400 mg + RTV 100 mg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ATV concentrations similar to (ATV 300 mg + RTV 100 mg) without EFV</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose</td>
<td>EFV standard dose</td>
<td>ETR standard dose</td>
<td>Do not coadminister.</td>
<td>Standard doses</td>
<td></td>
</tr>
<tr>
<td>In ART-Naive Patients:</td>
<td>(ATV 300 mg + RTV 100 mg)</td>
<td>(ATV 300 mg + RTV 100 mg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• ATV 400 mg + RTV 100 mg once daily</td>
<td>Once Daily:</td>
<td>Once Daily:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Do not coadminister.</td>
<td>• ETR AUC and (C_{\text{min}}) both ↑ ~30%</td>
<td>• ATV AUC ↔ and (C_{\text{min}}) ↓ 18%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DRV/c</td>
<td>PK Data</td>
<td>↓ DRV possible</td>
<td>↓ DRV possible</td>
<td>↓ DRV possible</td>
<td>↔ DRV expected</td>
</tr>
<tr>
<td>Dose</td>
<td>Do not coadminister.</td>
<td>Do not coadminister.</td>
<td>Do not coadminister.</td>
<td>Standard doses</td>
<td></td>
</tr>
</tbody>
</table>
Table 19a. Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitorsa  
(Last updated October 17, 2017; last reviewed October 17, 2017)  (Page 2 of 2)

<table>
<thead>
<tr>
<th>PIs</th>
<th>PK Data</th>
<th>EFV</th>
<th>ETR</th>
<th>NVP</th>
<th>RPVb</th>
</tr>
</thead>
</table>
| DRV/r | PK Data | With (DRV 300 mg + RTV 100 mg) BID:  
• EFV AUC ↑ 21%  
• DRV AUC ↓ 13% and Cmin ↓ 31%  
With (DRV 600 mg + RTV 100 mg) BID:  
• ETR AUC ↓ 37% and Cmin ↓ 49%  
• DRV: No significant change  
With (DRV 400 mg + RTV 100 mg) BID:  
• NVP AUC ↑ 27% and Cmin ↑ 47%  
• DRV AUC ↑ 24%b | ETR 100 mg BID with (DRV 600 mg + RTV 100 mg) BID:  
• ETR AUC ↓ 37% and Cmin ↓ 49%  
• DRV: No significant change | With (DRV 400 mg + RTV 100 mg) BID:  
• NVP AUC ↑ 27% and Cmin ↑ 47%  
• DRV AUC ↑ 24%b | RPV 150 mg Once Daily with (DRV 800 mg + RTV 100 mg) Once Daily:  
• RPV AUC ↑ 130% and Cmin ↑ 178%  
• DRV: No significant change |
| Dose | Clinical significance unknown. Use standard doses and monitor patient closely. Consider monitoring drug levels. | Standard doses | Despite reduced ETR concentration, safety and efficacy of this combination have been established in a clinical trial. | Standard doses | Standard doses |

| LPV/r | PK Data | With LPV/r Tablets 500/125 mg BID:  
• LPV concentration similar to that with LPV/r 400/100 mg BID without EFV  
With LPV/r Tablets:  
• ETR AUC ↓ 35% (comparable to the decrease with DRV/r)  
• LPV AUC ↓ 13% | With LPV/r Tablets:  
• ETR AUC ↓ 35% (comparable to the decrease with DRV/r)  
• LPV AUC ↓ 13% | With LPV/r Capsules:  
• LPV AUC ↓ 27% and Cmin ↓ 51% | RPV 150 mg Once Daily with LPV/r Capsules:  
• RPV AUC ↑ 52% and Cmin ↑ 74%  
• LPV: No significant change |
| Dose | LPV/r tablets 500/125 mg BID; LPV/r oral solution 533/133 mg BID  
EFV standard dose | Standard doses | LPV/r tablets 500/125 mg BID; LPV/r oral solution 533/133 mg BID  
NVP standard dose | Standard doses | Standard doses |

| TPV | PK Data | With (TPV 500 mg + RTV 100 mg) BID:  
• EFV ↔  
• TPV AUC ↓ 31% and Cmin ↓ 42%  
With (TPV 750 mg + RTV 200 mg) BID:  
• EFV and TPV: ↔ | With (TPV 500 mg + RTV 200 mg) BID:  
• ETR AUC ↓ 76% and Cmin ↓ 82%  
• TPV AUC ↑ 18% and Cmin ↑ 24% | With (TPV 250 mg + RTV 200 mg) BID or with (TPV 750 mg + RTV 100 mg) BID:  
• NVP: ↔  
• TPV: ↔ expected | ↑ RPV possible |
| Dose | Standard doses | Do not coadminister. | Standard doses | Standard doses |

---

a Approved dose for RPV is 25 mg once daily. Most PK studies were performed using 75 mg to 150 mg RPV per dose.

b Based on between-study comparison.

c Use a combination of two LPV/r 200/50 mg tablets plus one LPV/r 100/25 mg tablet to make a total dose of LPV/r 500/125 mg.

**Key to Symbols:**

↑ = increase  
↓ = decrease  
↔ = no change

**Key to Acronyms:** ART = antiretroviral therapy; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BID = twice daily; Cmin = minimum plasma concentration; COBI = cobicistat; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; EFV = efavirenz; ETR = etravirine; LPV = lopinavir; LPV/r = lopinavir/ritonavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PK = pharmacokinetic; RPV = rilpivirine; RTV = ritonavir; TPV = tipranavir
Table 19b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors (Last updated October 17, 2017; last reviewed October 17, 2017) (page 1 of 3)

Recommendations for managing a particular drug interaction may differ depending on whether a new ARV is being initiated in a patient on a stable concomitant medication, or if a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly.

<table>
<thead>
<tr>
<th>ARV Drugs by Drug Class</th>
<th>INSTIs</th>
<th>DTG</th>
<th>EVG/c</th>
<th>RAL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NNRTIs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EFV PK Data</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In Patients Without INSTI Resistance:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• DTG 50 mg BID</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In Patients With Certain INSTI-Associated Resistance* or Clinically Suspected INSTI Resistance:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Consider alternative combination.</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>DTG AUC ↓ 75% and C_{min} ↓ 75%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>↑ or ↓ EVG, COBI, EFV possible</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>With DTG 50 mg Once Daily:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With DTG 50 mg BID:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• RAL AUC ↓ 36% and C_{min} ↓ 21%</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>With RAL 1200 mg Once Daily:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• RAL AUC ↓ 14% and C_{min} ↔</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EFV PK Data</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ETR 200 mg BID + DTG 50 mg Once Daily:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• DTG AUC ↓ 71% and C_{min} ↓ 88%</td>
<td></td>
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</tr>
<tr>
<td>ETR 200 mg BID with (DRV 600 mg + RTV 100 mg) BID and DTG 50 mg Once Daily:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• DTG AUC ↓ 25% and C_{min} ↓ 37%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ETR 200 mg BID with (LPV 400 mg + RTV 100 mg) BID and DTG 50 mg Once Daily:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• DTG AUC ↑ 11% and C_{min} ↑ 28%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>↑ or ↓ EVG, COBI, ETR possible</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With RAL 400 mg BID:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• RAL C_{min} ↑ 17%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• RAL C_{min} ↓ 34%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do not coadminister.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAL 400 mg BID</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coadministration with RAL 1200 mg once daily is not recommended.</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>NVP PK Data</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With DTG 50 mg Once Daily:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• DTG AUC ↓ 19% and C_{min} ↓ 34%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>↑ or ↓ EVG, COBI, NVP possible</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No data</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Standard doses</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV

Downloaded from https://aidsinfo.nih.gov/guidelines on 8/8/2018
**Table 19b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors** *(Last updated October 17, 2017; last reviewed October 17, 2017) (page 2 of 3)*

<table>
<thead>
<tr>
<th>ARV Drugs by Drug Class</th>
<th>INSTIs</th>
<th>DTG</th>
<th>EVG/c</th>
<th>RAL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NNRTIs, continued</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>RPV</strong></td>
<td>PK Data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dose</td>
<td>Standard doses</td>
<td>Do not coadminister.</td>
<td>Standard doses</td>
</tr>
<tr>
<td><strong>NNRTIs, continued</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ATV/c</strong></td>
<td>PK Data</td>
<td>No data</td>
<td>ATV/c + EVG/c:</td>
<td>No data</td>
</tr>
<tr>
<td></td>
<td>Dose</td>
<td>Standard doses</td>
<td>Do not coadminister.</td>
<td>Standard doses</td>
</tr>
<tr>
<td><strong>ATV +/− RTV</strong></td>
<td>PK Data</td>
<td>Unboosted ATV + DTG 30 mg Once Daily:</td>
<td>↑ or ↓ EVG, COBI, ATV possible</td>
<td>With Unboosted ATV:</td>
</tr>
<tr>
<td></td>
<td>Dose</td>
<td>Standard doses</td>
<td>Do not coadminister.</td>
<td>Standard doses</td>
</tr>
<tr>
<td><strong>NNRTIs, continued</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>DRV/c</strong></td>
<td>PK Data</td>
<td>DTG 50 mg Once Daily and DRV/r Once Daily Switched to DRV/c:</td>
<td>DRV/c + EVG/c:</td>
<td>No data</td>
</tr>
<tr>
<td></td>
<td>Dose</td>
<td>Standard doses</td>
<td>Do not coadminister.</td>
<td>Standard doses</td>
</tr>
<tr>
<td><strong>NNRTIs, continued</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>DRV/r</strong></td>
<td>PK Data</td>
<td>(DRV 600 mg + RTV 100 mg) BID with DTG 30 mg Once Daily:</td>
<td>↑ or ↓ EVG, COBI, DRV possible</td>
<td>With (DRV 600 mg + RTV 100 mg) BID:</td>
</tr>
<tr>
<td></td>
<td>Dose</td>
<td>Standard doses</td>
<td>Do not coadminister.</td>
<td>Standard doses</td>
</tr>
<tr>
<td><strong>NNRTIs, continued</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>LPV/r</strong></td>
<td>PK Data</td>
<td>With (LPV 400 mg + RTV 100 mg) BID and DTG 30 mg Once Daily:</td>
<td>↑ or ↓ EVG, COBI, LPV possible</td>
<td>↓ RAL</td>
</tr>
<tr>
<td></td>
<td>Dose</td>
<td>Standard doses</td>
<td>Do not coadminister.</td>
<td>Standard doses</td>
</tr>
<tr>
<td><strong>NNRTIs, continued</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TPV/r</strong></td>
<td>PK Data</td>
<td>With (TPV 500 mg + RTV 200 mg) BID and DTG 50 mg Once Daily:</td>
<td>↑ or ↓ EVG, COBI, TPV possible</td>
<td>With (TPV 500 mg + RTV 200 mg) BID and RAL 400 mg BID:</td>
</tr>
<tr>
<td></td>
<td>Dose</td>
<td>In Patients Without INSTI Resistance:</td>
<td>Do not coadminister.</td>
<td>RAL 400 mg BID</td>
</tr>
</tbody>
</table>

| In Patients With Certain INSTI-Associated Resistance\(^a\) or Clinically Suspected INSTI Resistance: |
| Consider alternative combination. |

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV
Table 19b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors  (Last updated October 17, 2017; last reviewed October 17, 2017)  (page 3 of 3)

*a Refer to DTG product labeling for details.

**Key to Symbols:**

↑ = increase  
↓ = decrease  
↔ = no change

**Key to Acronyms:** ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BID = twice daily; Cmin = minimum plasma concentration; COBI = cobicistat; CYP = cytochrome P; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; INSTI = integrase strand transfer inhibitor; LPV = lopinavir; LPV/r = lopinavir/ritonavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PK = pharmacokinetic; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; TPV = tipranavir; TPV/r = tipranavir/ritonavir
## Appendix B, Table 1. Characteristics of Nucleoside Reverse Transcriptase Inhibitors  
( Last updated October 17, 2017; last reviewed October 17, 2017 )  
(page 1 of 6)

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation)</th>
<th>Trade Name</th>
<th>Formulations</th>
<th>Dosing Recommendations</th>
<th>Elimination</th>
<th>Serum/Intracellular Half-Lives</th>
<th>Adverse Events</th>
</tr>
</thead>
</table>
| **Abacavir** (ABC)          | Ziagen     | Ziagen:      | Ziagen:                | Metabolized by alcohol dehydrogenase and glucuronyl transferase Renal excretion of metabolites: 82% Dosage adjustment for ABC is recommended in patients with hepatic insufficiency (see Appendix B, Table 7). | 1.5 hours/12–26 hours | **HSRs:** Patients who test positive for HLA-B*5701 are at highest risk. HLA screening should be done before initiation of ABC.  
For patients with history of HSR, rechallenge is not recommended.  
Symptoms of HSR may include fever, rash, nausea, vomiting, diarrhea, abdominal pain, malaise, fatigue, or respiratory symptoms such as sore throat, cough, or shortness of breath.  
Some cohort studies suggest increased risk of MI with recent or current use of ABC, but this risk is not substantiated in other studies.  
**Insulin resistance/diabetes mellitus** |
| **Trazol (ABC/ZDV/3TC)**    | Note: Generic available.  
Also available as a component of fixed-dose combinations (by trade name and abbreviation): | Trazol: | Trazol: | 1 tablet BID | 1.5 hours/12–20 hours | **Pancreatitis**  
**Peripheral neuropathy**  
**Retinal changes, optic neuritis**  
**Lactic acidosis with hepatic steatosis with or without pancreatitis (rare but potentially life-threatening toxicity)**  
**Nausea, vomiting**  
**Potential association with noncirrhotic portal hypertension; in some cases, patients presented with esophageal varices**  
One cohort study suggested increased risk of MI with recent or current use of ddI, but this risk is not substantiated in other studies.  
**Insulin resistance/diabetes mellitus** |
| **Epzicom** (ABC/3TC)       | Note: Generic available. | Epzicom: | Epzicom: | 1 tablet once daily | 1.5 hours/20 hours | **Pancreatitis**  
**Peripheral neuropathy**  
**Retinal changes, optic neuritis**  
**Lactic acidosis with hepatic steatosis with or without pancreatitis (rare but potentially life-threatening toxicity)**  
**Nausea, vomiting**  
**Potential association with noncirrhotic portal hypertension; in some cases, patients presented with esophageal varices**  
One cohort study suggested increased risk of MI with recent or current use of ddI, but this risk is not substantiated in other studies.  
**Insulin resistance/diabetes mellitus** |
| **Trumeq** (ABC/3TC/DTG)    | Trumeq:    | Trumeq:      | Trumeq:                | Renal excretion: 50% Dosage adjustment in patients with renal insufficiency is recommended (see Appendix B, Table 7). | 1.5 hours/20 hours | **Pancreatitis**  
**Peripheral neuropathy**  
**Retinal changes, optic neuritis**  
**Lactic acidosis with hepatic steatosis with or without pancreatitis (rare but potentially life-threatening toxicity)**  
**Nausea, vomiting**  
**Potential association with noncirrhotic portal hypertension; in some cases, patients presented with esophageal varices**  
One cohort study suggested increased risk of MI with recent or current use of ddI, but this risk is not substantiated in other studies.  
**Insulin resistance/diabetes mellitus** |
| **Didanosine** (ddI)        | Videx      | Body Weight ≥60 kg: | Body Weight ≥60 kg: | | | **Insulin resistance/diabetes mellitus** |
|                             | Videx EC:  | 400 mg once daily | 400 mg once daily | | | |
|                             | 125, 200, 250, and 400 mg capsules | 250 mg once daily | 250 mg once daily | | | |
|                             | Videx:    | 10 mg/mL oral solution | 10 mg/mL oral solution | | | |
## Appendix B, Table 1. Characteristics of Nucleoside Reverse Transcriptase Inhibitors (Last updated October 17, 2017; last reviewed October 17, 2017) (page 2 of 6)

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation) Trade Name</th>
<th>Formulations</th>
<th>Dosing Recommendations</th>
<th>Elimination</th>
<th>Serum/Intracellular Half-Lives</th>
<th>Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emtricitabine (FTC) Emtriva</td>
<td>Emtriva:</td>
<td>Emtriva:</td>
<td>Renal excretion: 86%</td>
<td>10 hours/&gt;20 hours</td>
<td>• Minimal toxicity</td>
</tr>
<tr>
<td></td>
<td>• 200 mg hard gelatin capsule</td>
<td>Capsule: • 200 mg once daily</td>
<td>Dosage adjustment in patients with renal insufficiency is recommended (see Appendix B, Table 7).</td>
<td></td>
<td>• Hyperpigmentation/skin discoloration</td>
</tr>
<tr>
<td></td>
<td>• 10 mg/mL oral solution</td>
<td>Oral Solution: • 240 mg (24 mL) once daily</td>
<td></td>
<td></td>
<td>• Severe acute exacerbation of hepatitis may occur in patients with HBV/HIV coinfection who discontinue FTC.</td>
</tr>
<tr>
<td>Also available as a component of fixed-dose combinations (by trade name and abbreviation):</td>
<td>Atripla (FTC/EFV/TDF)</td>
<td>Atripla:</td>
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<td></td>
<td>Atripla:</td>
<td>Atripla:</td>
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<tr>
<td></td>
<td>• (FTC 200 mg + EFV 600 mg + TDF 300 mg) tablet</td>
<td>• 1 tablet at or before bedtime</td>
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<td></td>
<td>Truvada:</td>
<td>Truvada:</td>
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<tr>
<td></td>
<td>• (FTC 200 mg + TDF 300 mg) tablet</td>
<td>• 1 tablet once daily with a meal</td>
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<td></td>
<td>Complera:</td>
<td>Complera:</td>
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<td>Complera:</td>
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<td></td>
<td>• (FTC 200 mg + RPV 25 mg + TDF 300 mg) tablet</td>
<td>• 1 tablet once daily with a meal</td>
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<td></td>
<td>Descovy:</td>
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<td>Descovy:</td>
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<tr>
<td></td>
<td>• (FTC 200 mg + TAF 25 mg) tablet</td>
<td>• 1 tablet once daily</td>
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<td></td>
<td>Genvoya:</td>
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<td>Genvoya:</td>
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<tr>
<td></td>
<td>• (FTC 200 mg + EVG 150 mg + COBI 150 mg + TAF 10 mg) tablet</td>
<td>• 1 tablet once daily with food</td>
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<td></td>
<td>Odefsey:</td>
<td>Odefsey:</td>
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<td>Odefsey:</td>
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<tr>
<td></td>
<td>• (FTC 200 mg + RPV 25 mg + TAF 25 mg) tablet</td>
<td>• 1 tablet once daily with a meal</td>
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<td>Stribild:</td>
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<td>Stribild:</td>
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<tr>
<td></td>
<td>• (FTC 200 mg + EVG 150 mg + COBI 150 mg + TDF 300 mg) tablet</td>
<td>• 1 tablet once daily with food</td>
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<td></td>
<td>Truvada:</td>
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<td>Truvada:</td>
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<tr>
<td></td>
<td>• (FTC 200 mg + TDF 300 mg) tablet</td>
<td>• 1 tablet once daily</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Generic Name (Abbreviation) Trade Name</td>
<td>Formulations</td>
<td>Dosing Recommendations</td>
<td>Elimination</td>
<td>Serum/Intracellular Half-Lives</td>
<td>Adverse Events</td>
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</tr>
<tr>
<td>Lamivudine (3TC) Epivir</td>
<td>Epivir: • 150 and 300 mg tablets • 10 mg/mL oral solution</td>
<td>Epivir: • 300 mg once daily or • 150 mg BID Take without regard to meals.</td>
<td>Renal excretion: 70% Dosage adjustment in patients with renal insufficiency is recommended (see Appendix B, Table 7).</td>
<td>5–7 hours/18–22 hours</td>
<td>• Minimal toxicity • Severe acute exacerbation of hepatitis may occur in patients with HBV/HIV coinfection who discontinue 3TC.</td>
</tr>
<tr>
<td>Note: Generic available. Also available as a component of fixed-dose combinations (by trade name and abbreviation): Epivir: • 150 and 300 mg tablets • 10 mg/mL oral solution</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combivir (3TC/ZDV) Combivir: • (3TC 150 mg + ZDV 300 mg) tablet</td>
<td>Combivir: • 1 tablet BID</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Note: Generic available. Epzicom (3TC/ABC) Epzicom: • (3TC 300 mg + ABC 600 mg) tablet</td>
<td>Epzicom: • 1 tablet once daily</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Note: Generic available. Trizivir (3TC/ZDV/ABC) Trizivir: • (3TC 150 mg + ZDV 300 mg + ABC 300 mg) tablet</td>
<td>Trizivir: • 1 tablet BID</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Note: Generic available. Trizivir (3TC/ZDV/ABC) Trizivir: • (3TC 150 mg + ZDV 300 mg + ABC 300 mg) tablet</td>
<td>Trizivir: • 1 tablet BID</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triumeq (3TC/ABC/DTG) Triumeq: • (3TC 300 mg + ABC 600 mg + DTG 50 mg) tablet</td>
<td>Triumeq: • 1 tablet once daily</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Note: Generic available. Stavudine (d4T) Zerit: • 15, 20, 30, and 40 mg capsules • 1 mg/mL oral solution</td>
<td>Body Weight ≥60 kg: • 40 mg BID Body Weight &lt;60 kg: • 30 mg BID Take without regard to meals. Note: WHO recommends 30 mg BID dosing regardless of body weight.</td>
<td>Renal excretion: 50% Dosage adjustment in patients with renal insufficiency is recommended (see Appendix B, Table 7).</td>
<td>1 hour/7.5 hours</td>
<td></td>
<td>• Peripheral neuropathy • Lipoatrophy • Pancreatitis • Lactic acidosis/severe hepatomegaly with hepatic steatosis (rare but potentially life-threatening toxicity) • Hyperlipidemia • Insulin resistance/diabetes mellitus • Rapidly progressive ascending neuromuscular weakness (rare)</td>
</tr>
<tr>
<td>Generic Name (Abbreviation) Trade Name</td>
<td>Formulations</td>
<td>Dosing Recommendationsa</td>
<td>Elimination</td>
<td>Serum/Intracellular Half-Lives</td>
<td>Adverse Eventsb</td>
</tr>
<tr>
<td>---------------------------------------</td>
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</tr>
<tr>
<td>Tenofovir Alafenamide (TAF) Vemlidy</td>
<td>See fixed-dose combinations for HIV treatment below.</td>
<td>See fixed-dose combinations for HIV treatment below.</td>
<td>Metabolized by cathepsin A; P-glycoprotein substrate Not recommended in patients with CrCl &lt;30 mL/min.</td>
<td>0.5 hours/150–180 hours</td>
<td>• Renal insufficiency, Fanconi syndrome, proximal renal tubulopathy (less likely than from TDF) • Osteomalacia, decrease in bone mineral density (lesser effect than from TDF) • Severe acute exacerbation of hepatitis may occur in patients with HBV/HIV coinfection who discontinue TAF. • Diarrhea, nausea, headache</td>
</tr>
<tr>
<td><strong>Note:</strong> Available as a 25-mg tablet for the treatment of HBV.</td>
<td><strong>Fixed-dose combinations for HIV are listed below (by trade name and abbreviation):</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>Descovy (TAF/FTC)</strong></td>
<td>Descovy: • (FTC 200 mg + TAF 25 mg) tablet</td>
<td>Descovy: • 1 tablet once daily</td>
<td>0.5 hours/150–180 hours</td>
<td>0.5 hours/150–180 hours</td>
<td></td>
</tr>
<tr>
<td><strong>Genvoya (TAF/EVG/c/FTC)</strong></td>
<td>Genvoya: • (TAF 10 mg + EVG 150 mg + COBI 150mg + FTC 200 mg) tablet</td>
<td>Genvoya: • 1 tablet once daily with food</td>
<td>0.5 hours/150–180 hours</td>
<td>0.5 hours/150–180 hours</td>
<td></td>
</tr>
<tr>
<td><strong>Odefsey (TAF/RPV/FTC)</strong></td>
<td>Odefsey: • (TAF 25 mg + RPV 25 mg + FTC 200 mg) tablet</td>
<td>Odefsey: • 1 tablet once daily with a meal</td>
<td>0.5 hours/150–180 hours</td>
<td>0.5 hours/150–180 hours</td>
<td></td>
</tr>
</tbody>
</table>
### Appendix B, Table 1. Characteristics of Nucleoside Reverse Transcriptase Inhibitors  *(Last updated October 17, 2017; last reviewed October 17, 2017)*  (page 5 of 6)

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation)</th>
<th>Trade Name</th>
<th>Formulations</th>
<th>Dosing Recommendations*</th>
<th>Elimination</th>
<th>Serum/Intracellular Half-Lives</th>
<th>Adverse Eventsb</th>
</tr>
</thead>
</table>
| **Tenofovir Disoproxil Fumarate (TDF)** | **Viread** | **Viread:**  
- 150, 200, 250, and 300 mg tablets  
- 40 mg/g oral powder | **Viread:**  
- 300 mg once daily, or  
- 7.5 level scoops once daily (dosing scoop dispensed with each prescription; 1 level scoop contains 1 g of oral powder)  
- Mix oral powder with 2–4 ounces of a soft food that does not require chewing (e.g., applesauce, yogurt).  
**Do not mix oral powder with liquid.** | Renal excretion is primary route of elimination.  
Dosage adjustment in patients with renal insufficiency is recommended (see Appendix B, Table 7). | 17 hours/ >60 hours |  
- Renal insufficiency, Fanconi syndrome, proximal renal tubulopathy  
- Osteomalacia, decrease in bone mineral density  
- Severe acute exacerbation of hepatitis may occur in patients with HBV/HIV coinfection who discontinue TDF.  
- Asthenia, headache, diarrhea, nausea, vomiting, and flatulence |
| **Atripla (TDF/EFV/FTC)** | **Atripla:**  
- (TDF 300 mg + EFV 600 mg + FTC 200 mg) tablet | **Atripla:**  
- 1 tablet at or before bedtime  
- Take on an empty stomach to reduce side effects. |  |  |  |  |
| **Complera (TDF/RPV/FTC)** | **Complera:**  
- (TDF 300 mg + RPV 25 mg + FTC 200 mg) tablet | **Complera:**  
- 1 tablet once daily  
- Take with a meal. |  |  |  |  |
| **Stribild (TDF/EVG/c/FTC)** | **Stribild:**  
- (TDF 300 mg + EVG 150 mg + COBI 150 mg + FTC 200 mg) tablet | **Stribild:**  
- 1 tablet once daily  
- Take with food. |  |  |  |  |
| **Truvada (TDF/FTC)** | **Truvada:**  
- (TDF 300 mg + FTC 200 mg) tablet | **Truvada:**  
- 1 tablet once daily  
- Take without regard to meals. |  |  |  |  |

---

*Please refer to the guidelines for detailed dosing recommendations.

*bAdverse Events: Common side effects may include nausea, diarrhea, headache, and fatigue. More serious side effects may include bone density decrease, kidney problems, and severe hepatitis exacerbation.

Appendix B, Table 1. Characteristics of Nucleoside Reverse Transcriptase Inhibitors  *(Last updated October 17, 2017; last reviewed October 17, 2017)*  (page 5 of 6)
Appendix B, Table 1. Characteristics of Nucleoside Reverse Transcriptase Inhibitors  *(Last updated October 17, 2017; last reviewed October 17, 2017)*  (page 6 of 6)

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation) Trade Name</th>
<th>Formulations</th>
<th>Dosing Recommendations*</th>
<th>Elimination</th>
<th>Serum/Intracellular Half-Lives</th>
<th>Adverse Eventsb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zidovudine (ZDV) Retrovir</td>
<td></td>
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</tr>
<tr>
<td><strong>Note</strong>: Generic available.</td>
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<tr>
<td>Also available as a component of fixed-dose combinations (by trade name and abbreviation):</td>
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<tr>
<td>Corticosteroids:</td>
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<tr>
<td>Trizivir (ZDV/3TC/ABC)</td>
<td>Trizivir: (ZDV 300 mg + 3TC 150 mg + ABC 300 mg) tablet</td>
<td>Trizivir: 1 tablet BID</td>
<td>Take without regard to meals.</td>
<td>1.1 hours/7 hours</td>
<td>• Bone marrow suppression: macrocytic anemia or neutropenia</td>
</tr>
<tr>
<td><strong>Note</strong>: Generic available.</td>
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</tr>
<tr>
<td>Combivir (ZDV/3TC)</td>
<td>Combivir: (ZDV 300 mg + 3TC 150 mg) tablet</td>
<td>Combivir: 1 tablet BID</td>
<td>Take without regard to meals.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Note</strong>: Generic available.</td>
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</tr>
<tr>
<td>Zidovudine (ZDV) Retrovir</td>
<td>Retrovir: 100 mg capsule</td>
<td>Retrovir: 300 mg BID, or 200 mg TID</td>
<td>Metabolized to GAZT Renal excretion of GAZT Dosage adjustment in patients with renal insufficiency is recommended (see Appendix B, Table 7).</td>
<td>1.1 hours/7 hours</td>
<td></td>
</tr>
<tr>
<td><strong>Note</strong>: Generic available.</td>
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<tr>
<td>Also available as a component of fixed-dose combinations (by trade name and abbreviation):</td>
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</tr>
<tr>
<td>Combivir (ZDV/3TC)</td>
<td>Combivir: (ZDV 300 mg + 3TC 150 mg) tablet</td>
<td>Combivir: 1 tablet BID</td>
<td>Take without regard to meals.</td>
<td>1.1 hours/7 hours</td>
<td></td>
</tr>
<tr>
<td><strong>Note</strong>: Generic available.</td>
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</tr>
<tr>
<td>Trizivir (ZDV/3TC/ABC)</td>
<td>Trizivir: (ZDV 300 mg + 3TC 150 mg + ABC 300 mg) tablet</td>
<td>Trizivir: 1 tablet BID</td>
<td>Take without regard to meals.</td>
<td>1.1 hours/7 hours</td>
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</tr>
<tr>
<td><strong>Note</strong>: Generic available.</td>
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</tbody>
</table>

* For dosage adjustment in renal or hepatic insufficiency, see Appendix B, Table 7.

b Also see Table 14.

**Key to Acronyms**: 3TC = lamivudine; ABC = abacavir; BID = twice daily; COBI, c = cobicistat; CrCl = creatinine clearance; d4T = stavudine; ddI = didanosine; DTG = dolutegravir; EC = enteric coated; EFV = efavirenz; EVG = elvitegravir; FTC = emtricitabine; GAZT = azidothymidine glucuronide; HBV = hepatitis B virus; HLA = human leukocyte antigen; HSR = hypersensitivity reaction; MI = myocardial infarction; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TID = three times a day; WHO = World Health Organization; ZDV = zidovudine
Appendix B, Table 2. Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors  (Last updated October 17, 2017; last reviewed October 17, 2017)  (page 1 of 2)

Note: Delavirdine (DLV) is not included in this table. Please refer to the DLV Food and Drug Administration package insert for related information.

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation)</th>
<th>Trade Name</th>
<th>Formulations</th>
<th>Dosing Recommendations</th>
<th>Elimination/Metabolic Pathway</th>
<th>Serum Half-Life</th>
<th>Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Efavirenz (EFV)</strong> Sustiva</td>
<td></td>
<td>Sustiva:</td>
<td></td>
<td>Metabolized by CYPs 2B6 (primary), 3A4, and 2A6 CYP3A4 mixed inducer/inhibitor (more an inducer than an inhibitor) CYP2C9 and 2C19 inhibitor; 2B6 inducer</td>
<td>40–55 hours</td>
<td>• Rash&lt;sup&gt;c&lt;/sup&gt; • Neuropsychiatric symptoms&lt;sup&gt;d&lt;/sup&gt; • Hepatotoxicity • Hyperlipidemia • False-positive results with some cannabinoid and benzodiazepine screening assays reported. • Teratogenic in nonhuman primates • QT interval prolongation</td>
</tr>
<tr>
<td>Also available as a component of a fixed-dose combination (by trade name and abbreviation):</td>
<td></td>
<td>Atripla: (EFV/TDF/FTC)</td>
<td>Atripla: (EFV 600 mg + TDF 300 mg + FTC 200 mg) tablet</td>
<td>3A4 inducer; 2C9 and 2C19 inhibitor</td>
<td>41 hours</td>
<td>• Rash, including Stevens-Johnson syndrome&lt;sup&gt;c&lt;/sup&gt; • HSRs, characterized by rash, constitutional findings, and sometimes organ dysfunction (including hepatic failure) have been reported. • Nausea</td>
</tr>
<tr>
<td><strong>Etravirine (ETR)</strong> Intelence</td>
<td></td>
<td>• 25, 100, and 200 mg tablets</td>
<td>• 200 mg BID • Take following a meal.</td>
<td>CYP3A4, 2C9, and 2C19 substrate 3A4 inducer; 2C9 and 2C19 inhibitor</td>
<td>25–30 hours</td>
<td>• Rash, including Stevens-Johnson syndrome&lt;sup&gt;c&lt;/sup&gt; • Symptomatic hepatitis, including fatal hepatic necrosis, has been reported: • Rash reported in approximately 50% of cases. • Occurs at a significantly higher frequency in ARV-naive female patients with pre-NVP CD4 counts &gt;250 cells/mm&lt;sup&gt;3&lt;/sup&gt; and in ARV-naive male patients with pre-NVP CD4 counts &gt;400 cells/mm&lt;sup&gt;3&lt;/sup&gt;. NVP should not be initiated in these patients unless the benefit clearly outweighs the risk.</td>
</tr>
<tr>
<td><strong>Nevirapine (NVP)</strong> Viramune Viramune XR</td>
<td>Note: Generic available</td>
<td>• 200 mg tablet • 400 mg XR tablet • 50 mg/5 mL oral suspension</td>
<td>• 200 mg once daily for 14 days (lead-in period); thereafter, 200 mg BID, or 400 mg (Viramune XR tablet) once daily • Take without regard to meals. • Repeat lead-in period if therapy is discontinued for &gt;7 days. • In patients who develop mild-to-moderate rash without constitutional symptoms, continue lead-in period until rash resolves but not longer than 28 days total.</td>
<td>CYP450 substrate, inducer of 3A4 and 2B6; 80% excreted in urine (glucuronidated metabolites, &lt;5% unchanged); 10% excreted in feces</td>
<td>25–30 hours</td>
<td>• Rash, including Stevens-Johnson syndrome&lt;sup&gt;c&lt;/sup&gt; • Symptomatic hepatitis, including fatal hepatic necrosis, has been reported: • Rash reported in approximately 50% of cases. • Occurs at a significantly higher frequency in ARV-naive female patients with pre-NVP CD4 counts &gt;250 cells/mm&lt;sup&gt;3&lt;/sup&gt; and in ARV-naive male patients with pre-NVP CD4 counts &gt;400 cells/mm&lt;sup&gt;3&lt;/sup&gt;. NVP should not be initiated in these patients unless the benefit clearly outweighs the risk.</td>
</tr>
</tbody>
</table>
# Appendix B, Table 2. Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors (Last updated October 17, 2017; last reviewed October 17, 2017) (page 2 of 2)

**Note:** Delavirdine (DLV) is not included in this table. Please refer to the DLV Food and Drug Administration package insert for related information.

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation)</th>
<th>Formulations</th>
<th>Dosing Recommendations</th>
<th>Elimination/Metabolic Pathway</th>
<th>Serum Half-Life</th>
<th>Adverse Events&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rilpivirine (RPV)</strong></td>
<td>Edurant:</td>
<td>Edurant:</td>
<td>CYP3A4 substrate</td>
<td>50 hours</td>
<td>- Rash&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Edurant</strong></td>
<td>25 mg tablet</td>
<td>25 mg once daily</td>
<td></td>
<td></td>
<td>- Depression, insomnia, headache</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Take with a meal.</td>
<td></td>
<td></td>
<td>- Hepatotoxicity</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- QT interval prolongation</td>
</tr>
</tbody>
</table>

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**Also available as a component of fixed-dose combinations (by trade name and abbreviation):**

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation)</th>
<th>Formulations</th>
<th>Dosing Recommendations</th>
<th>Elimination/Metabolic Pathway</th>
<th>Serum Half-Life</th>
<th>Adverse Events&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Complera (RPV/TDF/FTC)</strong></td>
<td>Complera:</td>
<td>Complera:</td>
<td></td>
<td></td>
<td>- Rash&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>(RPV 25 mg + TDF 300 mg + FTC 200 mg) tablet</td>
<td>1 tablet once daily</td>
<td></td>
<td></td>
<td>- Depression, insomnia, headache</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Take with a meal.</td>
<td></td>
<td></td>
<td>- Hepatotoxicity</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- QT interval prolongation</td>
</tr>
</tbody>
</table>

---

**Odefsey (RPV/TAF/FTC)**

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation)</th>
<th>Formulations</th>
<th>Dosing Recommendations</th>
<th>Elimination/Metabolic Pathway</th>
<th>Serum Half-Life</th>
<th>Adverse Events&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odefsey:</td>
<td>Odefsey:</td>
<td></td>
<td></td>
<td>- Rash&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>(RPV 25 mg + TAF 25 mg + FTC 200 mg) tablet</td>
<td>1 tablet once daily</td>
<td></td>
<td></td>
<td>- Depression, insomnia, headache</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Take with a meal.</td>
<td></td>
<td></td>
<td>- Hepatotoxicity</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- QT interval prolongation</td>
</tr>
</tbody>
</table>

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<sup>a</sup> For dosage adjustment in renal or hepatic insufficiency, see Appendix B, Table 7.

<sup>b</sup> Also see Table 14.

<sup>c</sup> Rare cases of Stevens-Johnson syndrome have been reported with most NNRTIs; the highest incidence of rash was seen with NVP.

<sup>d</sup> Adverse events can include dizziness, somnolence, insomnia, abnormal dreams, depression, suicidality (suicide, suicide attempt or ideation), confusion, abnormal thinking, impaired concentration, amnesia, agitation, depersonalization, hallucinations, and euphoria. Approximately 50% of patients receiving EFV may experience any of these symptoms. Symptoms usually subside spontaneously after 2 to 4 weeks but may necessitate discontinuation of EFV in a small percentage of patients.

**Key to Acronyms:** ARV = antiretroviral; BID = twice daily; CD4 = CD4 T lymphocyte; CYP = cytochrome P; EFV = efavirenz; ETR = etravirine; FTC = emtricitabine; HSR = hypersensitivity reaction; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; XR = extended release.
### Appendix B, Table 3. Characteristics of Protease Inhibitors  (Last updated October 17, 2017; last reviewed October 17, 2017) (page 1 of 6)

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation) Trade Name</th>
<th>Formulations</th>
<th>Dosing Recommendationsa</th>
<th>Elimination/ Metabolic Pathway</th>
<th>Serum Half-Life</th>
<th>Storage</th>
<th>Adverse Eventsb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atazanavir (ATV) Reyataz</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Reyataz:</td>
<td>In ARV-Naive Patients:</td>
<td>CYP3A4 inhibitor and substrate; weak CYP2C8 inhibitor; UGT1A1 inhibitor</td>
<td>7 hours</td>
<td>Room temperature (up to 25º C or 77º F)</td>
<td>• Indirect hyperbilirubinemia</td>
</tr>
<tr>
<td></td>
<td>• 100, 150, 200, and 300 mg capsules</td>
<td>• (ATV 300 mg + RTV 100 mg) once daily; or</td>
<td>Dosage adjustment in patients with hepatic insufficiency is recommended (see Appendix B, Table 7).</td>
<td></td>
<td></td>
<td>• PR interval prolongation: First degree symptomatic AV block reported. Use with caution in patients with underlying conduction defects or in patients on concomitant medications that can cause PR prolongation.</td>
</tr>
<tr>
<td></td>
<td>• 50 mg single packet oral powder</td>
<td>• ATV 400 mg once daily</td>
<td></td>
<td></td>
<td></td>
<td>• Hyperglycemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>With TDF or in ARV- Experienced Patients:</td>
<td></td>
<td></td>
<td></td>
<td>• Fat maldistribution</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• (ATV 300 mg + RTV 100 mg) once daily</td>
<td></td>
<td></td>
<td></td>
<td>• Cholelithiasis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>With EFV in ARV-Naive Patients:</td>
<td></td>
<td></td>
<td></td>
<td>• Nephrolithiasis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• (ATV 400 mg + RTV 100 mg) once daily</td>
<td></td>
<td></td>
<td></td>
<td>• Renal insufficiency</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Take with food.</td>
<td></td>
<td></td>
<td></td>
<td>• Serum transaminase elevations</td>
</tr>
<tr>
<td></td>
<td></td>
<td>For recommendations on dosing with H2 antagonists and PPIs, refer to Table 18a.</td>
<td></td>
<td></td>
<td></td>
<td>• Hyperlipidemia (especially with RTV boosting)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Skin rash</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Increase in serum creatinine (with COBI)</td>
</tr>
<tr>
<td>Evotaz (ATV/c)</td>
<td>Evotaz:</td>
<td></td>
<td>ATV: As above COBI: substrate of CYP3A, CYP2D6 (minor); CYP3A inhibitor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• (ATV 300 mg + COBI 150 mg) tablet</td>
<td>• 1 tablet once daily</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Take with food.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>With TDF:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Not recommended for patients with baseline CrCl &lt;70 mL/min (see Appendix B, Table 7 for the equation for calculating CrCl).</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Darunavir (DRV) Prezista

**Generic Name (Abbriviation)** | **Trade Name**
---|---
Darunavir (DRV) | Prezista

**Formulations**
- 75, 150, 600, and 800 mg tablets
- 100 mg/mL oral suspension

**Dosing Recommendations**
- In ARV-Naive Patients or ARV-Experienced Patients with No DRV Mutations:
  - (DRV 800 mg + RTV 100 mg) once daily

- In ARV-Experienced Patients with 1 or More DRV Resistance Mutations:
  - (DRV 600 mg + RTV 100 mg) BID

Unboosted DRV is not recommended. Take with food.

**Elimination/Metabolic Pathway**
- CYP3A4 inhibitor and substrate
- CYP2C9 inducer

**Serum Half-Life**
- 15 hours (when combined with RTV)

**Storage**
- Room temperature (up to 25°C or 77°F)

**Adverse Events**
- Skin rash (10%): DRV has a sulfonamide moiety; Stevens-Johnson syndrome, toxic epidermal necrolysis, acute generalized exanthematous pustulosis, and erythema multiforme have been reported.
- Hepatotoxicity
- Diarrhea, nausea
- Headache
- Hyperlipidemia
- Serum transaminase elevation
- Hyperglycemia
- Fat maldistribution
- Increase in serum creatinine (with COBI)

**Also available as a fixed-dose combination (by trade name and abbreviation):**

<table>
<thead>
<tr>
<th><strong>Prezobix (DRV/c)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Prezobix:</td>
</tr>
<tr>
<td>- (DRV 800 mg + COBI 150 mg) tablet</td>
</tr>
</tbody>
</table>

**Formulations**
- Prezobix: 1 tablet once daily
- Take with food.

**Dosing Recommendations**
- Not recommended for patients with 1 or more DRV resistance-associated mutations.

**With TDF:**
- Not recommended for patients with baseline CrCl <70 mL/min (see Appendix B, Table 7 for the equation for calculating CrCl).

**Elimination/Metabolic Pathway**
- DRV: As above
- COBI: substrate of CYP3A, CYP2D6 (minor); CYP3A inhibitor

**Storage**
- Room temperature (up to 25°C or 77°F)
<table>
<thead>
<tr>
<th>Generic Name (Abbreviation)</th>
<th>Trade Name</th>
<th>Formulations</th>
<th>Dosing Recommendations</th>
<th>Elimination/ Metabolic Pathway</th>
<th>Serum Half-Life</th>
<th>Storage</th>
<th>Adverse Events</th>
</tr>
</thead>
</table>
| **Fosamprenavir (FPV)**    | **Lexiva** (a prodrug of APV) | • 700 mg tablet  
• 50 mg/mL oral suspension | **In ARV-Naive Patients:**  
• FPV 1400 mg BID, or  
• (FPV 1400 mg + RTV 100–200 mg) once daily, or  
• (FPV 700 mg + RTV 100 mg) BID | APV is a CYP3A4 substrate, inhibitor, and inducer.  
Dosage adjustment in patients with hepatic insufficiency is recommended (see Appendix B, Table 7). | 7.7 hours (APV) | Room temperature (up to 25º C or 77º F) | • Skin rash (12% to 19%): FPV has a sulfonamide moiety.  
• Diarrhea, nausea, vomiting  
• Headache  
• Hyperlipidemia  
• Serum transaminase elevation  
• Hyperglycemia  
• Fat maldistribution  
• Possible increased bleeding episodes in patients with hemophilia  
• Nephrolithiasis |
| **Indinavir (IDV)**     | **Crixivan** | • 100, 200, and 400 mg capsules  
• 800 mg every 8 hours  
• Take 1 hour before or 2 hours after meals; may take with skim milk or a low-fat meal.  
**With RTV:**  
• (IDV 800 mg + RTV 100–200 mg) BID  
• Take without regard to meals. | CYP3A4 inhibitor and substrate  
Dosage adjustment in patients with hepatic insufficiency is recommended (see Appendix B, Table 7). | 1.5–2 hours | Room temperature (15º to 30º C or 59º to 86º F) | Protect from moisture.  
• Nephrolithiasis  
• GI intolerance, nausea  
• Hepatitis  
• Indirect hyperbilirubinemia  
• Hyperlipidemia  
• Headache, asthenia, blurred vision, dizziness, rash, metallic taste, thrombocytopenia, alopecia, and hemolytic anemia  
• Hyperglycemia  
• Fat maldistribution  
• Possible increased bleeding episodes in patients with hemophilia |
### Appendix B, Table 3. Characteristics of Protease Inhibitors  
(Last updated October 17, 2017; last reviewed October 17, 2017)  
(page 4 of 6)

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation)</th>
<th>Trade Name</th>
<th>Formulations</th>
<th>Dosing Recommendations</th>
<th>Elimination/Metabolic Pathway</th>
<th>Serum Half-Life</th>
<th>Storage</th>
<th>Adverse Events</th>
</tr>
</thead>
</table>
| Lopinavir/Ritonavir (LPV/r) Kaletra | Tablets:  
• (LPV 200 mg + RTV 50 mg), or  
• (LPV 100 mg + RTV 25 mg)  
Oral Solution:  
• Each 5 mL contains (LPV 400 mg + RTV 100 mg), or  
• Oral solution contains 42% alcohol. | • (LPV 400 mg + RTV 100 mg) BID, or  
• (LPV 800 mg + RTV 200 mg) once daily  
Once-daily dosing is not recommended for patients with ≥3 LPV-associated mutations, pregnant women, or patients receiving EFV, NVP, FPV, NFV, carbamazepine, phenytoin, or phenobarbital.  
With EFV or NVP (PI-Naive or PI Experienced Patients):  
• LPV/r 500/125 mg tablets BID (use a combination of 2 LPV/r 200/50 mg tablets + 1 LPV/r 100/25 mg tablet to make a total dose of LPV/r 500/125 mg), or  
• LPV/r 533/133 mg oral solution BID  
Tablet:  
• Take without regard to meals.  
Oral Solution:  
• Take with food. | CYP3A4 inhibitor and substrate | 5–6 hours | Oral tablet is stable at room temperature.  
Oral solution is stable at 2º to 8º C (36º to 46º F) until date on label and is stable for up to 2 months when stored at room temperature (up to 25º C or 77º F). | • GI intolerance, nausea, vomiting, diarrhea  
• Pancreatitis  
• Asthenia  
• Hyperlipidemia (especially hypertriglyceridemia)  
• Serum transaminase elevation  
• Hyperglycemia  
• Insulin resistance/diabetes mellitus  
• Fat maldistribution  
• Possible increased bleeding episodes in patients with hemophilia  
• PR interval prolongation  
• QT interval prolongation and torsades de pointes have been reported; however, causality could not be established. |
| Nelfinavir (NFV) Viracept | • 250 and 625 mg tablets  
• 50 mg/g oral powder | • 1250 mg BID, or  
• 750 mg TID  
Dissolve tablets in a small amount of water, mix admixture well, and consume immediately.  
Take with food. | CYP2C19 and 3A4 substrate—metabolized to active M8 metabolite; CYP3A4 inhibitor | 3.5–5 hours | Room temperature (15º to 30º C or 59º to 86º F) | • Diarrhea  
• Hyperlipidemia  
• Hyperglycemia  
• Fat maldistribution  
• Possible increased bleeding episodes in patients with hemophilia  
• Serum transaminase elevation |
### Appendix B, Table 3. Characteristics of Protease Inhibitors  
**Last updated October 17, 2017; last reviewed October 17, 2017**  
(page 5 of 6)

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation) Tradename</th>
<th>Formulations</th>
<th>Dosing Recommendations&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Elimination/ Metabolic Pathway</th>
<th>Serum Half-Life</th>
<th>Storage</th>
<th>Adverse Events&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
</table>
| **Ritonavir (RTV)** Norvir           | • 100 mg tablet  
• 100 mg soft gel capsule  
• 80 mg/mL oral solution  
• 100 mg single-packet oral powder | As PK Booster (or Enhancer) for Other PIs:  
• 100–400 mg per day in 1 or 2 divided doses (refer to other PIs for specific dosing recommendations).  
*Tablet:*  
• Take with food.  
*Capsule and Oral Solution:*  
• To improve tolerability, take with food if possible. | CYP3A4 > 2D6 substrate; potent 3A4, 2D6 inhibitor; inducer of CYPs 1A2, 2C8, 2C9, and 2C19 and UGT1A1 | 3–5 hours | Tablets and oral powder do not require refrigeration.  
Refrigerate capsules.  
Capsules can be left at room temperature (up to 25º C or 77º F) for up to 30 days.  
**Oral solution should not be refrigerated.** | • GI intolerance, nausea, vomiting, diarrhea  
• Paresthesia (circumoral and extremities)  
• Hyperlipidemia (especially hypertriglyceridemia)  
• Hepatitis  
• Asthenia  
• Taste perversion  
• Hyperglycemia  
• Fat maldistribution  
• Possible increased bleeding episodes in patients with hemophilia |
| **Saquinavir (SQV)** Invirase        | • 500 mg tablet  
• 200 mg capsule | (SQV 1000 mg + RTV 100 mg) BID  
Unboosted SQV is not recommended.  
Take with meals or within 2 hours after a meal. | CYP3A4 substrate | 1–2 hours | Room temperature (15º to 30º C or 59º to 86º F) | • GI intolerance, nausea, and diarrhea  
• Headache  
• Serum transaminase elevation  
• Hyperlipidemia  
• Hyperglycemia  
• Fat maldistribution  
• Possible increased bleeding episodes in patients with hemophilia  
• PR interval prolongation  
• QT interval prolongation. Torsades de pointes have been reported. Patients with pre-SQV QT interval >450 msec should not receive SQV. |
### Appendix B, Table 3. Characteristics of Protease Inhibitors

(Last updated October 17, 2017; last reviewed October 17, 2017) (page 6 of 6)

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation)</th>
<th>Trade Name</th>
<th>Formulations</th>
<th>Dosing Recommendations</th>
<th>Elimination/ Metabolic Pathway</th>
<th>Serum Half-Life</th>
<th>Storage</th>
<th>Adverse Events</th>
</tr>
</thead>
</table>
| Tipranavir (TPV)            | Aptivus    | • 250 mg capsule  
• 100 mg/mL oral solution | • (TPV 500 mg + RTV 200 mg) BID  
Unboosted TPV is not recommended.  
With RTV Tablets:  
• Take with meals.  
With RTV Capsules or Solution:  
• Take without regard to meals.  
CYP P450 3A4 inducer and substrate  
CYP2D6 inhibitor; CYP3A4, 1A2, and 2C19 inducer  
Net effect when combined with RTV (CYP3A4, 2D6 inhibitor) | 6 hours after single dose of TPV/r | Refrigerate capsules.  
Capsules can be stored at room temperature (25º C or 77º F) for up to 60 days. | Oral solution should not be refrigerated or frozen and should be used within 60 days after bottle is opened.  
• Hepatotoxicity: Clinical hepatitis (including hepatic decompensation and hepatitis-associated fatalities) has been reported. Monitor patients closely, especially those with underlying liver diseases.  
• Skin rash (3% to 21%); TPV has a sulfonamide moiety; use with caution in patients with known sulfonamide allergy.  
• Rare cases of fatal and nonfatal intracranial hemorrhages have been reported. Risks include brain lesion, head trauma, recent neurosurgery, coagulopathy, hypertension, alcoholism, and the use of anticoagulant or antiplatelet agents (including vitamin E).  
• Hyperlipidemia  
• Hyperglycemia  
• Fat maldistribution  
• Possible increased bleeding episodes in patients with hemophilia |

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a For dosage adjustment in hepatic insufficiency, see Appendix B, Table 7.

b Also see Table 14.

**Key to Acronyms:** APV = amprenavir; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; AV = atrioventricular; BID = twice daily; COBI, c = cobicistat; CrCl = creatine clearance; CYP = cytochrome P; DRV = darunavir; DRV/c = darunavir/cobicistat; EFV = efavirenz; FPV = fosamprenavir; GI = gastrointestinal; IDV = indinavir; LPV = lopinavir; LPV/r = lopinavir/ritonavir; msec = millisecond; NFV = nelfinavir; NVP = nevirapine; PI = protease inhibitor; PPI = proton pump inhibitor; RTV = ritonavir; SQV = saquinavir; TDF = tenofovir disoproxil fumarate; TID = three times a day; TPV = tipranavir; TPV/r = tipranavir/ritonavir; UGT = uridine diphosphate glucuronosyltransferase
Appendix B, Table 4. Characteristics of Integrase Inhibitors  (Last updated October 17, 2017; last reviewed October 17, 2017)  (page 1 of 2)

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation) Trade Name</th>
<th>Formulations</th>
<th>Dosing Recommendationsa</th>
<th>Elimination/ Metabolic Pathways</th>
<th>Serum Half-Life</th>
<th>Adverse Eventsb</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dolutegravir (DTG) Tivicay</strong></td>
<td>• 50 mg tablet</td>
<td>ARV-Naive or ARV-Experienced, INSTI-Naive Patients: • 50 mg once daily ARV-Naive or ARV-Experienced, INSTI-Naive Patients when Coadministered with EFV, FPV/r, TPV/r, or Rifampin: • 50 mg BID INSTI-Experienced Patients with Certain INSTI Mutations (See Product Label) or with Clinically Suspected INSTI Resistance: • 50 mg BID</td>
<td>UGT1A1-mediated glucuronidation Minor contribution from CYP3A4</td>
<td>~14 hours</td>
<td>• HSRs, including rash, constitutional symptoms, and organ dysfunction (including liver injury) have been reported. • Insomnia • Headache • Depression and suicidal ideation (rare; usually in patients with pre-existing psychiatric conditions)</td>
</tr>
<tr>
<td><strong>Also available as a component of a fixed-dose combination (by trade name and abbreviation):</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Triumeq (DTG/ABC/3TC)</strong></td>
<td>Triumeq: (DTG 50 mg + ABC 600 mg + 3TC 300 mg) tablet</td>
<td>• Take 1 tablet daily without regard to meals.</td>
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<td></td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>Elvitegravir (EVG)</strong> Only available as a component of fixed-dose combinations (by trade name and abbreviation):</td>
<td>See fixed-dose combinations below.</td>
<td>See fixed-dose combinations below.</td>
<td>CYP3A, UGT1A1/3 substrate</td>
<td>~9 hours</td>
<td>• Nausea • Diarrhea • Depression and suicidal ideation (rare; usually in patients with pre-existing psychiatric conditions)</td>
</tr>
<tr>
<td><strong>Genvoya (EVG/c/FTC/TAF)</strong></td>
<td>Genvoya: (EVG 150 mg + COBI 150 mg + FTC 200 mg + TAF 10 mg) tablet</td>
<td>Genvoya: • 1 tablet once daily with food Not recommended for patients with CrCl &lt;30 mL/min (see Appendix B, Table 7 for the equation for calculating CrCl).</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Stribild (EVG/c/FTC/ TDF)</strong></td>
<td>Stribild: (EVG 150 mg + COBI 150 mg + FTC 200 mg + TDF 300 mg) tablet</td>
<td>Stribild: • 1 tablet once daily with food Not recommended for patients with baseline CrCl &lt;70 mL/min (see Appendix B, Table 7 for the equation for calculating CrCl).</td>
<td></td>
<td></td>
<td>~13 hours</td>
</tr>
</tbody>
</table>
### Appendix B, Table 4. Characteristics of Integrase Inhibitors

*(Last updated October 17, 2017; last reviewed October 17, 2017) (page 2 of 2)*

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation)</th>
<th>Trade Name</th>
<th>Formulations</th>
<th>Dosing Recommendations*</th>
<th>Elimination/ Metabolic Pathways</th>
<th>Serum Half-Life</th>
<th>Adverse Events†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raltegravir (RAL)</td>
<td>Isentress</td>
<td>• 400 mg tablet</td>
<td>ARV-Naive Patients or ARV- Experienced Patients: • Isentress: 400 mg BID</td>
<td>UGT1A1-mediated glucuronidation</td>
<td>~9 hours</td>
<td>• Rash, including Stevens-Johnson syndrome, HSR, and toxic epidermal necrolysis</td>
</tr>
<tr>
<td></td>
<td>Isentress HD</td>
<td>• 600 mg tablet (HD)</td>
<td>ARV-Naive or ARV- Experienced Patients who are Virologically Suppressed on a Regimen of RAL 400 mg BID: • Isentress HD: 1200 mg (two 600-mg tablets) once daily</td>
<td></td>
<td></td>
<td>• Nausea</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 25 and 100 mg chewable tablets</td>
<td>With Rifampin: • Isentress: 800 mg BID</td>
<td></td>
<td></td>
<td>• Headache</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 100 mg single packet for oral suspension</td>
<td>• Isentress HD: Not recommended</td>
<td></td>
<td></td>
<td>• Diarrhea</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Take without regard to meals.</td>
<td></td>
<td></td>
<td>• Pyrexia</td>
</tr>
</tbody>
</table>

* For dosage adjustment in hepatic insufficiency, see Appendix B, Table 7.

† Also see Table 14.

**Key to Acronyms:** 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; BID = twice daily; COBI, c = cobicistat; CPK = creatine phosphokinase; CrCl = creatinine clearance; CYP = cytochrome P; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; HSR = hypersensitivity reaction; INSTI = integrase strand transfer inhibitor; RAL = raltegravir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumerate; UGT = uridine diphosphate glucuronosyltransferase

### Appendix B, Table 5. Characteristics of Fusion Inhibitor

*(Last updated January 29, 2008; last reviewed October 17, 2017)*

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation)</th>
<th>Trade Name</th>
<th>Formulation</th>
<th>Dosing Recommendation</th>
<th>Serum Half-Life</th>
<th>Elimination</th>
<th>Storage</th>
<th>Adverse Events*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enfuvirtide (T20)</td>
<td>Fuzeon</td>
<td>• Injectable; supplied as lyophilized powder</td>
<td>• 90 mg (1 mL) subcutaneously BID</td>
<td>3.8 hours</td>
<td>Expected to undergo catabolism to its constituent amino acids, with subsequent recycling of the amino acids in the body pool.</td>
<td>Store at room temperature (up to 25º C or 77º F). Reconstituted solution should be refrigerated at 2º to 8º C (36º to 46º F) and used within 24 hours.</td>
<td>• Local injection site reactions (e.g., pain, erythema, induration, nodules and cysts, pruritus, ecchymosis) occur in almost 100% of patients</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Each vial contains 108 mg of T20; reconstitute with 1.1 mL of sterile water for injection for delivery of approximately 90 mg/1 mL.</td>
<td></td>
<td></td>
<td></td>
<td>• Increased incidence of bacterial pneumonia</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• HSR (&lt;1% of patients). Symptoms may include rash, fever, nausea, vomiting, chills, rigor, hypotension, or elevated serum transaminases. Rechallenge is not recommended.</td>
<td></td>
</tr>
</tbody>
</table>

* Also see Table 14.

**Key to Abbreviations:** BID = twice daily; HSR = hypersensitivity reaction; T20 = enfuvirtide

*Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV*
### Appendix B, Table 6. Characteristics of CCR5 Antagonist  (Last updated March 27, 2012; last reviewed October 17, 2017)

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation) Trade Name</th>
<th>Formulations</th>
<th>Dosing Recommendationsa</th>
<th>Serum Half-Life</th>
<th>Elimination/Metabolic Pathway</th>
<th>Adverse Eventsb</th>
</tr>
</thead>
</table>
| Maraviroc (MVC) Selzentry            | • 150 and 300 mg tablets | • **150 mg BID** when given with drugs that are strong CYP3A inhibitors (with or without CYP3A inducers) including PIs (except TPV/r)  
• **300 mg BID** when given with NRTIs, T20, TPV/r, NVP, RAL, and other drugs that are not strong CYP3A inhibitors or inducers  
• **600 mg BID** when given with drugs that are CYP3A inducers, including EFV, ETR, etc. (without a CYP3A inhibitor)  
Take without regard to meals. | 14–18 hours | CYP3A4 substrate | • Abdominal pain  
• Cough  
• Dizziness  
• Musculoskeletal symptoms  
• Pyrexia  
• Rash  
• Upper respiratory tract infections  
• Hepatotoxicity, which may be preceded by severe rash or other signs of systemic allergic reactions  
• Orthostatic hypotension, especially in patients with severe renal insufficiency |

*a For dosage adjustment in hepatic insufficiency, see Appendix B, Table 7.

*b Also see Table 14.

**Key to Acronyms:** BID = twice daily; CYP = cytochrome P; EFV = efavirenz; ETR = etravirine; MVC = maraviroc; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; RAL = raltegravir; T20 = enfuvirtide; TPV/r = tipranavir/ritonavir
Appendix B, Table 7. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency  (Last updated October 17, 2017; last reviewed October 17, 2017)  (page 1 of 6)

See the reference section at the end of this table for CrCl calculation formulas and criteria for Child-Pugh classification.

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation) Trade Name</th>
<th>Usual Daily Dosea</th>
<th>Dosing in Renal Insufficiencyb</th>
<th>Dosing in Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NRTIs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stribild should not be initiated in patients with CrCl &lt;70 mL/min. Use of the following fixed-dose combinations is not recommended in patients with CrCl &lt;50 mL/min: Atripla, Combivir, Complera, Epzicom, Triumeq, or Trizivir. Descovy, Genvoya, Odefsey, and Truvada are not recommended in patients with CrCl &lt;30 mL/min.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abacavir (ABC) Zidovudine</td>
<td>300 mg PO BID</td>
<td>No dosage adjustment necessary</td>
<td>Child-Pugh Class A:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• 200 mg PO BID (use oral solution)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Child-Pugh Class B or C:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Contraindicated</td>
</tr>
<tr>
<td>Didanosine EC (ddI) Videx EC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abacavir</td>
<td>300 mg PO BID</td>
<td>No dosage adjustment necessary</td>
<td></td>
</tr>
<tr>
<td></td>
<td>300 mg PO once daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>250 mg PO once daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Didanosine Oral Solution (ddI) Videx</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emtricitabine (FTC) Emtriva</td>
<td>200 mg oral capsule once daily, or 240 mg (24 mL) oral solution once daily</td>
<td>No dosage recommendation</td>
<td></td>
</tr>
<tr>
<td>Lamivudine (3TC) Epivir</td>
<td>300 mg PO once daily, or 150 mg PO BID</td>
<td>No dosage adjustment necessary</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stavudine (d4T) Zerit</td>
<td>40 mg PO BID</td>
<td>No dosage recommendation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>30 mg PO BID</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dose (Once Daily)</th>
<th>CrCl (mL/min)</th>
<th>≥60 kg</th>
<th>&lt;60 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–59</td>
<td>200 mg</td>
<td>125 mg</td>
<td></td>
</tr>
<tr>
<td>10–29</td>
<td>125 mg</td>
<td>125 mg</td>
<td></td>
</tr>
<tr>
<td>&lt;10, HD,c CAPD</td>
<td>125 mg</td>
<td>75 mg</td>
<td>oral solution</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dose (Once Daily)</th>
<th>CrCl (mL/min)</th>
<th>≥60 kg</th>
<th>&lt;60 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–59</td>
<td>200 mg</td>
<td>150 mg</td>
<td></td>
</tr>
<tr>
<td>10–29</td>
<td>150 mg</td>
<td>100 mg</td>
<td></td>
</tr>
<tr>
<td>&lt;10, HD,c CAPD</td>
<td>100 mg</td>
<td>75 mg</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dose (Once Daily)</th>
<th>CrCl (mL/min)</th>
<th>Capsule</th>
<th>Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–49</td>
<td>200 mg q48h</td>
<td>120 mg q24h</td>
<td></td>
</tr>
<tr>
<td>15–29</td>
<td>200 mg q72h</td>
<td>80 mg q24h</td>
<td></td>
</tr>
<tr>
<td>&lt;15 or on HDc</td>
<td>200 mg q96h</td>
<td>60 mg q24h</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dose (Once Daily)</th>
<th>CrCl (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–49</td>
<td>150 mg</td>
<td>q24h</td>
</tr>
<tr>
<td>15–29</td>
<td>1 x 150 mg, then 100 mg q24h</td>
<td></td>
</tr>
<tr>
<td>5–14</td>
<td>1 x 150 mg, then 50 mg q24h</td>
<td></td>
</tr>
<tr>
<td>&lt;5 or on HDc</td>
<td>1 x 50 mg, then 25 mg q24h</td>
<td></td>
</tr>
</tbody>
</table>

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### Appendix B, Table 7. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency

**Last updated October 17, 2017; last reviewed October 17, 2017**

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation) Trade Name</th>
<th>Usual Daily Dosea</th>
<th>Dosing in Renal Insufficiencyb</th>
<th>Dosing in Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NRTIs, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Tenofovir Alafenamide/Emtricitabine (TAF/FTC) Descovy | TAF available as a component of fixed-dose combinations for HIV (i.e., Descovy, Genvoya, and Odefsey) • TAF 10 mg PO daily with EVG/c (Genvoya), or • TAF 25 mg PO daily in other fixed-dose combinations | | Child-Pugh Class A or B: • No dosage adjustment  
Child-Pugh Class C: • No dosage recommendation  |
| Tenofovir Disoproxil Fumarate (TDF) Viread | • 300 mg PO once daily | **CrCl (mL/min)** | **Dose** | No dosage adjustment necessary |
| Tenofovir Disoproxil Fumarate/Emtricitabine (TDF/FTC) Truvada | • 1 tablet PO once daily | **CrCl (mL/min)** | **Dose** | No dosage recommendation |
| Zidovudine (ZDV) Retrovir | • 300 mg PO BID | **CrCl (mL/min)** | **Dose** | No dosage recommendation |
| **NNRTIs**                              |                   |                               |                               |
| Efavirenz (EFV) Sustiva | • 600 mg PO once daily, at or before bedtime | No dosage adjustment necessary | Child-Pugh Class A: • No dosage adjustment  
Child-Pugh Class B or C: • Not recommended  |
| Efavirenz/Tenofovir Disoproxil Fumarate/Emtricitabine (EFV/TDF/FTC) Atripla | • 1 tablet PO once daily | Not recommended for use in patients with CrCl <50 mL/min. Instead, use the individual drugs of the fixed-dose combination and adjust TDF and FTC doses according to CrCl level. |   |
| Etravirine (ETR) Intelence | • 200 mg PO BID | No dosage adjustment necessary | Child-Pugh Class A or B: • No dosage adjustment  
Child-Pugh Class C: • No dosage recommendation  |
| Nevirapine (NVP) Viramune Viramune XR | • 200 mg PO BID, or • 400 mg PO once daily (using Viramune XR formulation) | Patients on HD: • Limited data; no dosage recommendation | Child-Pugh Class A: • No dosage adjustment  
Child-Pugh Class B or C: • Contraindicated  |

---

**CrCl (ml/min)**
- <30 or on HD: Not recommended
- Child-Pugh Class A or B:
  - No dosage adjustment
  - Child-Pugh Class C:
    - No dosage recommendation
- Child-Pugh Class A:
  - No dosage adjustment
  - Child-Pugh Class B or C: Not recommended
- Child-Pugh Class A or B:
  - No dosage adjustment
  - Child-Pugh Class C: No dosage recommendation
- Child-Pugh Class A: No dosage adjustment
  - Child-Pugh Class B or C: No dosage recommendation
- Child-Pugh Class A: No dosage adjustment
  - Child-Pugh Class B or C: Contraindicated

---

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## Appendix B, Table 7. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency

(last updated October 17, 2017; last reviewed October 17, 2017)  (page 3 of 6)

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation)</th>
<th>Usual Daily Dose</th>
<th>Dosing in Renal Insufficiency</th>
<th>Dosing in Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NNRTIs, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rilpivirine (RPV) Edurant</td>
<td>25 mg PO once daily</td>
<td>No dosage adjustment necessary</td>
<td>Child-Pugh Class A or B: No dosage adjustment Child-Pugh Class C: No dosage recommendation</td>
</tr>
<tr>
<td>Rilpivirine/Tenofovir Alafenamide/Emtricitabine (RPV/TAF/FTC) Odefsey</td>
<td>1 tablet PO once daily</td>
<td><strong>Not recommended</strong> for use in patients with CrCl &lt;30 mL/min</td>
<td>Child-Pugh Class A or B: No dosage adjustment Child-Pugh Class C: No dosage recommendation</td>
</tr>
<tr>
<td>Rilpivirine/Tenofovir Disoproxil Fumarate/Emtricitabine (RPV/TDF/FTC) Complera</td>
<td>1 tablet PO once daily</td>
<td><strong>Not recommended</strong> for use in patients with CrCl &lt;50 mL/min. Instead, use the individual drugs of the fixed-dose combination and adjust TDF and FTC doses according to CrCl level.</td>
<td>Child-Pugh Class A or B: No dosage adjustment Child-Pugh Class C: No dosage recommendation</td>
</tr>
<tr>
<td><strong>PIs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atazanavir (ATV) Reyataz</td>
<td>400 mg PO once daily, or (ATV 300 mg + RTV 100 mg) PO once daily</td>
<td>No dosage adjustment for patients with renal dysfunction who do not require HD. ARV-Naive Patients on HD: (ATV 300 mg + RTV 100 mg) PO once daily ARV- Experienced Patients on HD: ATV or ATV/r not recommended.</td>
<td>Child-Pugh Class B: 300 mg once daily Child-Pugh Class C: Not recommended RTV boosting is not recommended in patients with hepatic impairment.</td>
</tr>
<tr>
<td>Atazanavir/Cobicistat (ATV/c) Evotaz</td>
<td>1 tablet PO once daily</td>
<td>If Used with TDF: Not recommended for use in patients with CrCl &lt;70 mL/min</td>
<td>Not recommended in patients with hepatic impairment</td>
</tr>
<tr>
<td>Darunavir (DRV) Prezista</td>
<td>ARV-Naive Patients and ARV- Experienced Patients with No DRV Resistance Mutations: (DRV 800 mg + RTV 100 mg) PO once daily ARV- Experienced Patients with at Least 1 DRV Resistance Mutation: (DRV 600 mg + RTV 100 mg) PO BID</td>
<td>No dosage adjustment necessary</td>
<td>Mild-to-Moderate Hepatic Impairment: No dosage adjustment Severe Hepatic Impairment: Not recommended</td>
</tr>
</tbody>
</table>
## Appendix B, Table 7. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency

(Last updated October 17, 2017; last reviewed October 17, 2017)

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation)</th>
<th>Trade Name</th>
<th>Usual Daily Dose&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Dosing in Renal Insufficiency&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Dosing in Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PIs, continued</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| **Darunavir/Cobicistat**    | Prezcobix  | • 1 tablet PO once daily (only recommended for patients without DRV-associated resistance mutations) | If Used with TDF:  
• Not recommended for use in patients with CrCl <70 mL/min | Child-Pugh Class A or B:  
• No dosage adjustment  
Child-Pugh Class C:  
• Not recommended |
| **Fosamprenavir**           | Lexiva     | • 1400 mg PO BID, or  
• (FPV 1400 mg + RTV 100–200 mg) PO once daily, or  
• (FPV 700 mg + RTV 100 mg) PO BID | No dosage adjustment necessary | PI-Naive Patients Only  
Child-Pugh Score 5–9:  
• 700 mg BID  
Child-Pugh Score 10–15:  
• 350 mg BID  
PI-Naive or PI-Experienced Patients  
Child-Pugh Score 5–6:  
• (700 mg BID + RTV 100 mg) once daily  
Child-Pugh Score 7–9:  
• (450 mg BID + RTV 100 mg) once daily  
Child-Pugh Score 10–15:  
• (300 mg BID + RTV 100 mg) once daily |
| **Indinavir**               | Crixivan   | • 800 mg PO q8h | No dosage adjustment necessary | Mild-to-Moderate Hepatic Insufficiency Because of Cirrhosis:  
• 600 mg q8h |
| **Lopinavir/Ritonavir**     | Kaletra    | • (LPV 400 mg + RTV 100 mg) PO BID, or  
• (LPV 800 mg + RTV 200 mg) PO once daily | Avoid once-daily dosing in patients on HD | No dosage recommendation; use with caution in patients with hepatic impairment. |
| **Nelfinavir**              | Viracept   | • 1250 mg PO BID | No dosage adjustment necessary | Mild Hepatic Impairment:  
• No dosage adjustment  
Moderate-to-Severe Hepatic Impairment:  
• Do not use |
| **Ritonavir**               | Norvir     | As a PI-Boosting Agent:  
• 100–400 mg per day | No dosage adjustment necessary | Refer to recommendations for the primary PI. |
| **Saquinavir**              | Invirase   | • (SQV 1000 mg + RTV 100 mg) PO BID | No dosage adjustment necessary | Mild-to-Moderate Hepatic Impairment:  
• Use with caution  
Severe Hepatic Impairment:  
• Contraindicated |
### Appendix B, Table 7. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency

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<table>
<thead>
<tr>
<th>Generic Name (Abbreviation) Trade Name</th>
<th>Usual Daily Dosea</th>
<th>Dosing in Renal Insufficiencyb</th>
<th>Dosing in Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PIs, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tipranavir (TPV) Aptivus</td>
<td>(TPV 500 mg + RTV 200 mg) PO BID</td>
<td>No dosage adjustment necessary</td>
<td>Child-Pugh Class A:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Use with caution</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Child-Pugh Class B or C:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Contraindicated</td>
</tr>
<tr>
<td><strong>INSTIs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dolutegravir (DTG) Tivicay</td>
<td>• 50 mg once daily, or 50 mg BID</td>
<td>No dosage adjustment necessary</td>
<td>Child-Pugh Class A or B:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• No dosage adjustment</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Child-Pugh Class C:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Not recommended</td>
</tr>
<tr>
<td>Elvitegravir/ Cobicistat/ Tenofovir Alafenamide/ Emtricitabine (EVG/c/TAF/FTC) Genvoya</td>
<td>• 1 tablet once daily</td>
<td>Not recommended for use in patients with CrCl &lt;30 mL/min.</td>
<td>Mild-to-Moderate Hepatic Insufficiency:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• No dosage adjustment necessary</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Severe Hepatic Insufficiency:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Not recommended</td>
</tr>
<tr>
<td>Elvitegravir/ Cobicistat/ Tenofovir Disoproxil Fumarate/ Emtricitabine (EVG/c/TDF/FTC) Stribild</td>
<td>• 1 tablet once daily</td>
<td>EVG/c/TDF/FTC <strong>should not be initiated</strong> in patients with CrCl &lt;70 mL/min. Discontinue EVG/c/TDF/FTC if CrCl declines to &lt;50 mL/min while patient is on therapy.</td>
<td>Mild-to-Moderate Hepatic Insufficiency:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• No dosage adjustment necessary</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Severe Hepatic Insufficiency:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Not recommended</td>
</tr>
<tr>
<td>Raltegravir (RAL) Isentress Isentress HD</td>
<td>• 400 mg BID (using Isentress formulation), or 1200 mg once daily (use Isentress HD formulation only) Do not substitute Isentress tablets for Isentress HD dosage.</td>
<td>No dosage adjustment necessary</td>
<td>Mild-to-Moderate Hepatic Insufficiency:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• No dosage adjustment necessary</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Severe Hepatic Insufficiency:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• No recommendation</td>
</tr>
<tr>
<td><strong>Fusion Inhibitor</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enfuvirtide (T20) Fuzeon</td>
<td>• 90 mg subcutaneous BID</td>
<td>No dosage adjustment necessary</td>
<td>No dosage adjustment necessary</td>
</tr>
<tr>
<td><strong>CCR5 Antagonist</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Maraviroc (MVC) Selzentry</td>
<td></td>
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<td></td>
<td>The recommended dose differs based on concomitant medications and potential for drug-drug interactions. See Appendix B, Table 6 for detailed dosing information.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CrCl &lt;30 mL/min or on HD:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Without Potent CYP3A Inhibitors or Inducers:</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• 300 mg BID; reduce to 150 mg BID if postural hypotension occurs.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>With Potent CYP3A Inducers or Inhibitors:</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Not recommended</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>No dosage recommendations. Concentrations will likely be increased in patients with hepatic impairment.</td>
</tr>
</tbody>
</table>
Appendix B, Table 7. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency *(Last updated October 17, 2017; last reviewed October 17, 2017)* (page 6 of 6)

* Refer to Appendix B, Tables 1–6 for additional dosing information.
* Including with chronic ambulatory peritoneal dialysis and hemodialysis.
* On dialysis days, take dose after HD session.

**Key to Acronyms:** 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; ATV = atazanavir; ATV/r = atazanavir/ritonavir; AZT = zidovudine; BID = twice daily; COBI, c = cobicistat; CAPD = chronic ambulatory peritoneal dialysis; CrCl = creatinine clearance; CYP = cytochrome P; d4T = stavudine; ddI = didanosine; DRV = darunavir; DTG = dolutegravir; EC = enteric coated; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; FPV = fosamprenavir; FTC = emtricitabine; HD = hemodialysis; IDV = indinavir; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NFV = neflavin; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PO = orally; q(n)d = every (n) days; q(n)h = every (n) hours; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQV = saquinavir; T20 = enfuvirtide; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TID = three times daily; TPV = tipranavir; XR = extended release; ZDV = zidovudine
### Child-Pugh Score

<table>
<thead>
<tr>
<th>Component</th>
<th>Points Scored</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Encephalopathy*</td>
<td>None</td>
</tr>
<tr>
<td>Ascites</td>
<td>None</td>
</tr>
<tr>
<td>Albumin</td>
<td>&gt;3.5 g/dL</td>
</tr>
<tr>
<td>Total bilirubin or</td>
<td>&lt;2 mg/dL (&lt;34 μmol/L)</td>
</tr>
<tr>
<td>Modified total bilirubinb</td>
<td>&lt;4 mg/dL</td>
</tr>
<tr>
<td>Prothrombin time (seconds prolonged) or</td>
<td>&lt;4</td>
</tr>
<tr>
<td>International normalized ratio (INR)</td>
<td>&lt;1.7</td>
</tr>
</tbody>
</table>

* Encephalopathy Grades
  - **Grade 1**: Mild confusion, anxiety, restlessness, fine tremor, slowed coordination
  - **Grade 2**: Drowsiness, disorientation, asterixis
  - **Grade 3**: Somnolent but rousable, marked confusion, incomprehensible speech, incontinence, hyperventilation
  - **Grade 4**: Coma, decerebrate posturing, flaccidity

b Modified total bilirubin used for patients who have Gilbert’s syndrome or who are taking indinavir or atazanavir

### Child-Pugh Classification

<table>
<thead>
<tr>
<th>Child-Pugh Classification</th>
<th>Total Child-Pugh Scorea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class A</td>
<td>5–6 points</td>
</tr>
<tr>
<td>Class B</td>
<td>7–9 points</td>
</tr>
<tr>
<td>Class C</td>
<td>&gt;9 points</td>
</tr>
</tbody>
</table>

*a Sum of points for each component of the Child-Pugh Score