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

Downloaded from https://aidsinfo.nih.gov/guidelines on 7/3/2020

Visit the AIDSinfo website to access the most up-to-date guideline.

Register for e-mail notification of guideline updates at https://aidsinfo.nih.gov/e-news.
# 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 (ARV) agents 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 50 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 Resources and 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 of HIV treatment and care. The U.S. government representatives are appointed by their respective agencies; other Panel members are selected after an open 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="https://aidsinfo.nih.gov/guidelines">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 to manage HIV infection. The <a href="https://aidsinfo.nih.gov/guidelines">latest version of the Financial Disclosure list</a> is available on the AIDSinfo website.</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 or data available in FDA drug labels. 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="https://aidsinfo.nih.gov/guidelines">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) for adults and adolescents with HIV. For a more detailed discussion on the use of ART in children and prepubertal adolescents (those with sexual maturity ratings of 1 to 3), clinicians should refer to the <a href="https://aidsinfo.nih.gov/guidelines">Pediatric Antiretroviral Guidelines</a>. These guidelines also include a brief discussion on the management of women of reproductive age and pregnant women. For more details on the use of ARV drugs during pregnancy, see the <a href="https://aidsinfo.nih.gov/guidelines">Perinatal Guidelines</a>.</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 relating to ARV drugs that may have an impact on the clinical care of persons with HIV. 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.</td>
</tr>
<tr>
<td><strong>Public comments</strong></td>
<td>A 2-week public comment period follows the release of the updated guidelines on the AIDSinfo website. The Panel reviews comments 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>A:</td>
<td>Strong recommendation for the statement</td>
</tr>
<tr>
<td>B:</td>
<td>Moderate recommendation for the statement</td>
</tr>
<tr>
<td>C:</td>
<td>Optional recommendation for the statement</td>
</tr>
<tr>
<td>I:</td>
<td>One or more randomized trials with clinical outcomes and/or validated laboratory endpoints</td>
</tr>
<tr>
<td>II:</td>
<td>One or more well-designed, non-randomized trials or observational cohort studies with long-term clinical outcomes</td>
</tr>
<tr>
<td>III:</td>
<td>Expert opinion</td>
</tr>
</tbody>
</table>
Table 3. Laboratory Testing Schedule for Monitoring People with HIV Before and After Initiation of Antiretroviral Therapy

<table>
<thead>
<tr>
<th>Laboratory Test</th>
<th>Timepoint or Frequency of Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Entry Into Care</td>
</tr>
<tr>
<td>HIV Serology</td>
<td>√</td>
</tr>
<tr>
<td></td>
<td>If HIV diagnosis has not been confirmed</td>
</tr>
<tr>
<td>CD4 Cell Count</td>
<td>√</td>
</tr>
<tr>
<td></td>
<td>√</td>
</tr>
<tr>
<td></td>
<td>√</td>
</tr>
<tr>
<td>HIV Viral Load</td>
<td>√</td>
</tr>
<tr>
<td></td>
<td>√</td>
</tr>
<tr>
<td></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></td>
<td>If considering a CCR5 antagonist</td>
</tr>
</tbody>
</table>

\(^a\) HIV diagnosis has not been confirmed; \(^b\) ART initiation; \(^c\) ART initiation is delayed; \(^d\) If CD4 count <300 cells/mm\(^3\) or increased by >100 cells/mm\(^3\) with ART; \(^e\) If CD4 count is <300 cells/mm\(^3\) or increased by >100 cells/mm\(^3\) with ART; \(^f\) Resistance testing can be performed at any time; \(^g\) If considering ABC; \(^h\) If considering a CCR5 antagonist, or for patients experiencing virologic failure on a CCR5 antagonist-based regimen.
Table 3. Laboratory Testing Schedule for Monitoring People with HIV Before and After Initiation of Antiretroviral Therapy*

<table>
<thead>
<tr>
<th>Laboratory Test</th>
<th>Timepoint or Frequency of Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hepatitis B Serology</strong> (HBsAb, HBsAg, HBcAb total)*</td>
<td>√</td>
</tr>
<tr>
<td><strong>ART Initiation</strong> or Modification</td>
<td>√</td>
</tr>
<tr>
<td><strong>2 to 8 Weeks After ART Initiation or Modification</strong></td>
<td>√</td>
</tr>
<tr>
<td><strong>Every 3 to 6 Months</strong></td>
<td>√</td>
</tr>
<tr>
<td><strong>Every 6 Months</strong></td>
<td>√</td>
</tr>
<tr>
<td><strong>Every 12 Months</strong></td>
<td>√</td>
</tr>
<tr>
<td><strong>Treatment Failure</strong></td>
<td>√</td>
</tr>
<tr>
<td><strong>Clinically Indicated</strong></td>
<td>√</td>
</tr>
<tr>
<td><strong>If ART Initiation is Delayed</strong></td>
<td>√</td>
</tr>
<tr>
<td><strong>Hepatitis C Screening</strong> (HCV antibody or, if indicated, HCV RNA)**</td>
<td>√</td>
</tr>
<tr>
<td><strong>Entry Into Care</strong></td>
<td>√</td>
</tr>
<tr>
<td><strong>ART Initiation or Modification</strong></td>
<td>√</td>
</tr>
<tr>
<td><strong>2 to 8 Weeks After ART Initiation or Modification</strong></td>
<td>√</td>
</tr>
<tr>
<td><strong>Every 3 to 6 Months</strong></td>
<td>√</td>
</tr>
<tr>
<td><strong>Every 6 Months</strong></td>
<td>√</td>
</tr>
<tr>
<td><strong>Every 12 Months</strong></td>
<td>√</td>
</tr>
<tr>
<td><strong>Treatment Failure</strong></td>
<td>√</td>
</tr>
<tr>
<td><strong>Clinically Indicated</strong></td>
<td>√</td>
</tr>
<tr>
<td><strong>If ART Initiation is Delayed</strong></td>
<td>√</td>
</tr>
<tr>
<td><strong>Basic Chemistry</strong></td>
<td>√</td>
</tr>
<tr>
<td><strong>ALT, AST, Total Bilirubin</strong></td>
<td>√</td>
</tr>
<tr>
<td><strong>CBC with Differential</strong></td>
<td>√</td>
</tr>
<tr>
<td><strong>Random or Fasting Lipid Profile</strong></td>
<td>√</td>
</tr>
<tr>
<td><strong>Random or Fasting Glucose</strong></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](https://aidsinfo.nih.gov/guidelines) on 7/3/2020
Table 3. Laboratory Testing Schedule for Monitoring People with HIV Before and After Initiation of Antiretroviral Therapya

<table>
<thead>
<tr>
<th>Laboratory Test</th>
<th>Entry Into Care</th>
<th>ART Initiationb 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>Urinalysismp,q</td>
<td>√</td>
<td>√</td>
<td></td>
<td>√</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnancy Testr</td>
<td>√</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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](https://aidsinfo.nih.gov/guidelines) for guidance on other laboratory tests generally recommended for primary health care maintenance of HIV patients.1

If ART is initiated 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 2–8 weeks, repeat testing every 4–8 weeks until viral load is suppressed to <200 copies/mL. Thereafter, repeat testing every 3–6 months.

In patients on ART, viral load typically is measured every 3–4 months. More frequent monitoring may be considered in individuals who are having difficulties with ART adherence. 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 or if a person presents with viremia while on an INSTI, 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 patients with virologic suppression who are switching therapy because of toxicity or for convenience, viral amplification will not be possible; see the section on Drug Resistance Testing for discussion of the potential limitations and benefits of proviral DNA assays in this situation. 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 result), TDF or TAF plus either FTC or 3TC should be used as part of the ARV regimen to treat both HBV and HIV infections (HBV/HIV).

If HBsAg, HBsAb, and HBCAb test results are negative, hepatitis B vaccine series should be administered. Refer to the [HIV Primary Care Guidelines](https://aidsinfo.nih.gov/guidelines) and the [Adult and Adolescent Opportunistic Infection Guidelines](https://aidsinfo.nih.gov/guidelines) for detailed recommendations.1,2

Most patients with isolated HBCAb have resolved HBV infection with loss of HBsAb. Consider performing an HBV viral load test for confirmation. If the HBV viral load test is positive, the patient may be acutely infected (and will usually display other signs of acute hepatitis) or chronically infected. If the test is negative, the patient should be vaccinated. Refer to the [HIV Primary Care Guidelines](https://aidsinfo.nih.gov/guidelines) and the [Adult and Adolescent Opportunistic Infection Guidelines](https://aidsinfo.nih.gov/guidelines) for more detailed recommendations.1,2

The HCV antibody test may not be adequate for screening in the setting of recent HCV infection (defined as acquisition within the past 6 months), or advanced immunodeficiency (CD4 count <100 cells/mm³). 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.

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 7/3/2020
<table>
<thead>
<tr>
<th>Laboratory Tests</th>
<th>Frequency of Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Na, K, HCO$_3^-$, Cl, BUN, creatinine, glucose, and creatinine-based estimated glomerular filtration rate. Serum phosphorus should be monitored in patients with chronic kidney disease who are on TDF-containing regimens. $^3$</td>
<td>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).</td>
</tr>
<tr>
<td>CBC with differential should be done when a CD4 count is performed. When CD4 count is no longer being monitored, the recommended frequency of CBC with differential is once a year. More frequent monitoring may be indicated for persons who are receiving medications that potentially cause cytopenia (e.g., ZDV, TMP-SMX). $^3$</td>
<td></td>
</tr>
<tr>
<td>If random lipids are abnormal, fasting lipids should be obtained. Consult the 2018 Guideline on the Management of Blood Cholesterol for diagnosis and management of patients with dyslipidemia. $^4$</td>
<td></td>
</tr>
<tr>
<td>If random glucose is abnormal, fasting glucose should be obtained. HbA1C is no longer recommended for diagnosis of diabetes in persons with HIV on ART (see the ADA Guidelines). $^5$</td>
<td></td>
</tr>
<tr>
<td>Urine glucose and protein should be assessed before initiating TAF- or TDF-containing regimens and monitored during treatment with these regimens. $^3$</td>
<td></td>
</tr>
</tbody>
</table>

Key: 3TC = lamivudine; ABC = abacavir; ALT = alanine aminotransferase; ART = antiretroviral therapy; ARV = antiretroviral; AST = aspartate aminotransferase; BUN = blood urea nitrogen; CBC = complete blood count; CD4 = CD4 T lymphocyte; Cl = chloride; DAA = direct-acting antiviral; FTC = emtricitabine; HbA1C = hemoglobin A1c; 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; TMP-SMX = trimethoprim-sulfamethoxazole; ZDV = zidovudine
Table 4. Recommendations on the Indications and Frequency of Viral Load and CD4 Count Monitoring

<table>
<thead>
<tr>
<th>Clinical Scenario</th>
<th>Viral Load Monitoring</th>
<th>CD4 Count Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Before initiating ART</strong></td>
<td>At entry into care (AIII)</td>
<td>At entry into care (AI)</td>
</tr>
<tr>
<td></td>
<td>If ART initiation is deferred, repeat before initiating ART (AIII).</td>
<td>If ART is deferred, every 3 to 6 monthsb (AIII)</td>
</tr>
<tr>
<td></td>
<td>In patients not initiating ART, repeat testing is optional (CIII).</td>
<td></td>
</tr>
<tr>
<td><strong>After initiating ART</strong></td>
<td>Preferably within 2 to 4 weeks (and no later than 8 weeks) after initiation of ART (AIII); thereafter, every 4 to 8 weeks until viral load is suppressed (BIII).</td>
<td>3 months after initiation of ART (AIII)</td>
</tr>
<tr>
<td><strong>After modifying ART because of drug toxicities or for regimen simplification in a patient with viral suppression</strong></td>
<td>4 to 8 weeks after modification of ART to confirm effectiveness of new regimen (AIII).</td>
<td>Monitor according to prior CD4 count and duration on ART, as outlined below.</td>
</tr>
<tr>
<td><strong>After modifying ART because of virologic failure</strong></td>
<td>Preferably within 2 to 4 weeks (and no later than 8 weeks) after modification (AIII); thereafter, every 4 to 8 weeks until viral load is suppressed (BIII). If viral suppression is not possible, repeat viral load every 3 months or more frequently if indicated (AIII).</td>
<td>Every 3 to 6 months (AII)</td>
</tr>
<tr>
<td><strong>During the first 2 years of ART</strong></td>
<td>Every 3 to 4 months (AIII)</td>
<td>Every 3 to 6 months (BII)</td>
</tr>
<tr>
<td>After 2 years of ART (VL consistently suppressed, CD4 consistently 300-500 cells/mm³)</td>
<td>Can extend to every 6 months for patients with consistent viral suppression for ≥2 years (AIII).</td>
<td>Optional (CIII)</td>
</tr>
<tr>
<td>After 2 years of ART (VL consistently suppressed, CD4 consistently &gt;500 cells/mm³)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>While on ART with detectable viremia (VL repeatedly &gt;200 copies/mL)</strong></td>
<td>Every 3 months (AIII) or more frequently if clinically indicated (see Virologic Failure).</td>
<td>Every 3 to 6 months (AIII)</td>
</tr>
<tr>
<td><strong>Change in clinical status (e.g., new HIV clinical symptom or initiation of interferon, chronic systemic corticosteroids, or antineoplastic therapy)</strong></td>
<td>Every 3 months (AIII)</td>
<td>Perform CD4 count and repeat as clinically indicatedc (AIII)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

b Some experts may repeat CD4 count every 3 months in patients with low baseline CD4 count (<200–300 cells/mm³) before ART but every 6 months in those who initiated ART at higher CD4 cell count (e.g., >300 cells/mm³).

c 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></td>
<td>Drug-resistance testing can determine whether drug-resistant virus was transmitted. The initial regimen can be modified, if necessary, 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.</td>
</tr>
<tr>
<td>Drug-resistance testing is recommended (AII). A genotypic assay is generally preferred (AIII).</td>
<td>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>If ART is deferred, repeat resistance testing may be considered when therapy is initiated (CIII). A genotypic assay is generally preferred (AIII).</td>
<td></td>
</tr>
<tr>
<td><strong>In ART-Naive Patients with Chronic HIV:</strong></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 to ARVs in the prescribed regimen. Some drug-resistance mutations can remain detectable for years in untreated patients with chronic HIV.</td>
</tr>
<tr>
<td>Drug-resistance testing is recommended at entry into HIV care to guide selection of initial ART (AII). A genotypic assay is generally preferred (AIII).</td>
<td>If necessary, the ART regimen can be modified once resistance test results are available.</td>
</tr>
<tr>
<td>For pregnant persons, or if ART will be initiated on the day of or soon after HIV diagnosis, treatment can be initiated prior to receiving resistance testing results.</td>
<td></td>
</tr>
<tr>
<td>If an INSTI is considered for an ART-naive patient and/or transmitted INSTI resistance is a concern, providers should supplement standard resistance testing with a specific INSTI genotypic resistance assay, which may need to be ordered separately (AIII).</td>
<td>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.</td>
</tr>
<tr>
<td>If therapy is deferred, repeat resistance testing may be considered before initiation of ART (CIII). A genotypic assay is generally preferred (AIII).</td>
<td>Repeat testing before initiation of ART may be considered because the patient may have acquired a drug-resistant virus (i.e., a superinfection).</td>
</tr>
<tr>
<td>If use of a CCR5 antagonist is being considered, a co-receptor tropism assay should be performed (AII).</td>
<td>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. See Co-Receptor Tropism Assays section.</td>
</tr>
<tr>
<td><strong>In Patients with Virologic Failure:</strong></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.</td>
</tr>
<tr>
<td>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).</td>
<td>The absence of detectable resistance in such patients must be interpreted with caution when designing subsequent ARV regimens, as mutations may decay with time.</td>
</tr>
<tr>
<td>Resistance testing should be done while the patient is taking ART or, if that is not possible, within 4 weeks after ART discontinuation (AII). If &gt;4 weeks have elapsed, resistance testing may still be useful to guide therapy; however, previously-selected mutations can be missed due to lack of drug selective pressure (CIII).</td>
<td>Drug resistance mutations may decay with time, and mutations detected in prior resistance tests may not be detected in current tests, though they remain clinically relevant.</td>
</tr>
<tr>
<td>A standard genotypic resistance assay is generally preferred for patients experiencing virologic failure on their first or second regimens and for those with noncomplex resistance patterns (AII).</td>
<td>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.</td>
</tr>
<tr>
<td>All prior and current drug-resistance testing results should be reviewed and considered when designing a new regimen for a patient experiencing virologic failure (AII).</td>
<td></td>
</tr>
<tr>
<td>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).</td>
<td>Genotypic assays provide information on resistance to NRTIs, NNRTIs, PIs, and INSTI-associated mutations. In some circumstances, INSTI resistance tests need to be ordered separately (clinicians should check with the testing laboratory).</td>
</tr>
</tbody>
</table>

*Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV*
Table 5. Recommendations for Using Drug-Resistance Assays (page 2 of 2)

<table>
<thead>
<tr>
<th>Clinical Setting and Recommendation</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adding phenotypic testing to genotypic testing is generally preferred in patients with known or suspected complex drug-resistance patterns (BIII).</td>
<td>Phenotypic testing can provide additional useful information in patients with complex drug resistance mutation patterns.</td>
</tr>
<tr>
<td>In Patients with Suboptimal Suppression of Viral Load: 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 in suboptimal viral suppression, and it can help the clinician identify the number of active drugs available in the current regimen and assess the need for a new regimen.</td>
</tr>
</tbody>
</table>

In Pregnant Persons with HIV:
Genotypic resistance testing is recommended for all pregnant persons before initiation of ART (AIII) and for those entering pregnancy with detectable HIV RNA levels while on therapy (AI).

The goals of ART in pregnant persons with HIV are to achieve maximal viral suppression for treatment of maternal HIV and to prevent 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, if needed.

In Patients with Undetectable Viral Load or Low-Level Viremia:
HIV-1 proviral DNA resistance assays may be useful in patients with HIV RNA below the limit of detection or with low-level viremia, where a HIV RNA genotypic assay is unlikely to be successful (CIII).

This test may provide information about previously circulating resistant viral variants that are archived within proviral DNA. These assays may miss some or all prior resistance mutations that have occurred within the viral quasi-species, and therefore they should be interpreted with caution. The clinical utility of HIV-1 proviral DNA assays has not been fully determined.

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 6a. Recommended Antiretroviral Regimens for Initial Therapy

Selection of a regimen should be individualized based on virologic efficacy, potential adverse effects, childbearing potential and use of effective contraception, 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.

**INSTI plus 2 NRTIs:**
- BIC/TAF/FTC (AI)
- DTG/ABC/3TC (AI)—if HLA-B*5701 negative
- DTG plus (TAF or TDF)* plus (FTC or 3TC) (AI)
- RAL plus (TAF or TDF) plus (FTC or 3TC) (BI for TDF/FTC or 3TC), BII for TAF/FTC

**INSTI plus 1 NRTI:**
- DTG/3TC (AI), except for individuals with HIV RNA >500,000 copies/mL, HBV coinfection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available

**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).

**INSTI plus 2 NRTIs:**
- EVG/c/(TAF or TDF)/FTC (BI)

**Boosted PI plus 2 NRTIs:**
- In general, boosted DRV is preferred over boosted ATV
- (DRV/c or DRV/r) plus (TAF or TDF)* plus (FTC or 3TC) (AI)
- (ATV/c or ATV/r) plus (TAF or TDF)* plus (FTC or 3TC) (BI)
- (DRV/c or DRV/r) plus ABC/3TC— if HLA-B*5701 negative (BII)

**NNRTI plus 2 NRTIs:**
- DOR/TDF/3TC (BI) or DOR plus TAF/FTC (BIII)
- EFV plus (TAF or TDF)* plus (FTC or 3TC)
- EFV 600 mg plus TDF plus (FTC or 3TC) (BI)
- EFV 400 mg TDF/3TC (BI)
- EVF 600 mg plus TAF/FTC (BII)
- RPV/(TAF or TDF)/FTC (BI)—if HIV RNA <100,000 copies/mL and CD4 count >200 cells/mm³

**Regimens to Consider when ABC, TAF, and TDF Cannot be Used or Are Not Optimal:**
- DTG/3TC (AI), except for individuals with HIV RNA >500,000 copies/mL, HBV coinfection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available
- DRV/r plus RAL twice a day (CI)—if HIV RNA <100,000 copies/mL and CD4 count >200 cells/mm³
- DRV/r once daily plus 3TC* (CI)

### Rating of Recommendations:

A = Strong; B = Moderate; C = Optional

### Rating of Evidence:

I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials, observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies, or regimen comparisons from randomized switch studies; III = Expert opinion

* TAF and TDF are two forms of TFV approved by 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.
Table 6a. Recommended Antiretroviral Regimens for Initial Therapy (page 2 of 2)

Note: The following are available as coformulated drugs: ABC/3TC, ATV/c, BIC/TAF/FTC, DOR/TDF/3TC, DRV/c, DRV/c/TAF/FTC, DTG/3TC, DTG/ABC/3TC, EFV (400 mg or 600 mg)/TDF/3TC, EFV/TDF/FTC, EVG/c/TAF/FTC, EVG/c/TDF/FTC, RPV/TAF/FTC, RPV/TDF/FTC, TAF/FTC, TDF/3TC, and TDF/FTC.

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; CD4 = CD4 T lymphocyte; DOR = doravirine; 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; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; RAL = raltegravir; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir; TDF/FTC, TAF/FTC, TDF/3TC, and TDF/FTC.

Table 6b. Considerations Before Initiating Dolutegravir and Other Integrase Strand Transfer Inhibitors as Initial Therapy for Persons of Childbearing Potential

**Background:**
- Preliminary data from a study in Botswana suggested that there is an increased risk of NTDs (0.9%) in infants born to women who were receiving DTG at the time of conception.\(^5\) Updated results have shown that the prevalence of NTDs in infants who were exposed to DTG at the time of conception is lower (0.3%) than reported in the preliminary data, but still higher than in infants who were exposed to ART that did not contain DTG (0.1%).\(^4\)
- There is limited data on RAL use around the time of conception. Thus far, based on data collected from the Antiretroviral Pregnancy Registry, the drug manufacturer, and in a cohort study from the United States and other countries, no case of NTD has been reported.\(^10,12\) Among those receiving RAL during pregnancy, the rate of fetal malformations is within the expected range for pregnancy outcomes in the United States.\(^10,12\)

**Before Initiating an INSTI-Containing Regimen in a Person of Childbearing Potential:**
- A pregnancy test should be performed (AIII).
- To enable individuals of childbearing potential to make informed decisions, providers should discuss the benefits and risks of using DTG around the time of conception, including the low risk of NTDs and the relative lack of information on the safety of using other commonly prescribed ARV drugs, including other INSTIs, around the time of conception (AIII).
- For individuals who are trying to conceive, the Panel recommends initiating one of the following regimens, which are designated as Preferred regimens during pregnancy in the Perinatal Guidelines: RAL, ATV/r or DRV/r plus TDF/FTC, TDF/3TC, or ABC/3TC. DTG would be an Alternative, rather than a Preferred, option (BII).
- For individuals who are not planning to conceive but who are sexually active and not using contraception, consider a regimen’s effectiveness and tolerability, the available data on potential teratogenicity, and the person’s preferences (e.g., low pill burden) when choosing among regimens recommended for initial therapy (Table 6a). In this situation, DTG would be an Alternative, rather than Preferred, option (BII). If the person becomes pregnant, changes to the ARV regimen may be warranted. Clinicians should refer to the Perinatal Guidelines for recommendations.
- For individuals who are using effective contraception, a DTG-based regimen is one of the recommended options; however, clinicians should discuss the risks and benefits of using DTG with patients to allow them to make an informed decision (AIII).
- An approach similar to that outlined for DTG should be considered for BIC-containing ART (AIII).
- EVG/c should not be used during pregnancy because of inadequate drug concentrations in the second and third trimesters (AII).
- Clinicians should refer to the Perinatal Guidelines when prescribing ART for a pregnant person with HIV.

**Rating of Recommendations:** A = Strong; B = Moderate; C = Optional

**Rating of Evidence:** I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials, observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies, or regimen comparisons from randomized switch studies; III = Expert opinion

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ATV = atazanavir; ATV/r = atazanavir/ritonavir; BIC = bictegravir; 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; NTD = neural tube defect; RAL = raltegravir; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir; TDF/FTC, TAF/FTC, TDF/3TC, and TDF/FTC.
Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios (page 1 of 4)

This table guides 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 9 for additional information regarding the advantages and disadvantages of particular ARV medications. Before initiating an INSTI-based regimen in a person of childbearing potential, review Table 6b for considerations in choosing the regimen.

<table>
<thead>
<tr>
<th>Pre-ART Characteristics</th>
<th>Clinical Scenario</th>
<th>Consideration(s)</th>
<th>Rationale/Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CD4 count &lt;200 cells/mm³</td>
<td>Do Not Use the Following Regimens:</td>
<td>A higher rate of virologic failure has been observed in those with low pretreatment CD4 counts.</td>
</tr>
<tr>
<td></td>
<td>HIV RNA &gt;100,000 copies/mL (also see next row if HIV RNA &gt;500,000 copies/mL)</td>
<td>Do Not Use the Following Regimens:</td>
<td>Higher rates of virologic failure have been observed in those with high pretreatment HIV RNA levels</td>
</tr>
<tr>
<td></td>
<td>HIV RNA &gt;500,000 copies/mL</td>
<td>Do Not Use the Following Regimens:</td>
<td>For DTG/3TC, limited data are available in patients above this viral load threshold.</td>
</tr>
<tr>
<td></td>
<td>HLA-B*5701 positive or result unknown</td>
<td>Do not use ABC-containing regimens.</td>
<td>ABC hypersensitivity, a potentially fatal reaction, is highly associated with the presence of the HLA-B*5701 allele.</td>
</tr>
<tr>
<td></td>
<td>ARV should be started before HIV drug resistance results are available (e.g., in a person with acute HIV) or when ART is being initiated rapidly.</td>
<td>Avoid NNRTI-based regimens and DTG/3TC. Avoid ABC.</td>
<td>Transmitted mutations conferring NNRTI and NRTI resistance are more likely than mutations associated with PI or INSTI resistance. HLA-B*5701 results may not be available rapidly. Transmitted resistance to DRV, BIC, and DTG is rare, and these drugs have high barriers to resistance.</td>
</tr>
<tr>
<td></td>
<td>ART-Specific Characteristics</td>
<td>STR Options as Initial ART Include:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>A one-pill, once-daily regimen is desired</td>
<td>BIC/TAF/FTC</td>
<td>Do not use DTG/ABC/3TC if patient is HLA-B*5701 positive.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DOR/TDF/3TC</td>
<td>DTG/3TC is not recommended if HIV RNA is &gt;500,000 copies/mL.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DRV/TAF/FTC</td>
<td>Do not use DTG/ABC/3TC or DTG/3TC in the setting of HBV coinfection or unknown HBV status.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DTG/ABC/3TC</td>
<td>Do not use RPV-based regimens if HIV RNA is &gt;100,000 copies/mL and CD4 count is &lt;200/mm³. See Appendix B, Table 10 for ARV dose recommendations in the setting of renal impairment.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DTG/3TC</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>EFV/TDF/FTC</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>EFV/TDF/3TC</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>EVGc/TAF/FTC</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>EVGc/TDF/FTC</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>RPV/TAF/FTC</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>RPV/TDF/FTC</td>
<td></td>
</tr>
</tbody>
</table>
### Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios

<table>
<thead>
<tr>
<th>Patient or Regimen Characteristics, continued</th>
<th>Clinical Scenario</th>
<th>Consideration(s)</th>
<th>Rationale/Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Food effects</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regimens that Can be Taken Without Regard to Food:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• BIC-, DOR-, DTG-, or RAL-based regimens</td>
<td></td>
<td></td>
<td>Oral bioavailability of these regimens is not significantly affected by food.</td>
</tr>
<tr>
<td><strong>Regimens that Should be Taken with Food:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• ATV/r- or ATV/c-based regimens</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• DRV/r- or DRV/c-based regimens</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• EVG/c/TAF/FTC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• EVG/c/TDF/FTC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• RPV-based regimens</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Regimens that Should be Taken on an Empty Stomach:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• EFV-based regimens</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Presence of Other Conditions</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic kidney disease (defined as CrCl &lt;60 mL/min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In general, avoid TDF.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABC may be used if patient is HLA-B*5701 negative. If HIV RNA is &gt;100,000 copies/mL, do not use ABC/3TC plus (EFV or ATV/r).</td>
<td></td>
<td></td>
<td>TDF has been associated with proximal renal tubulopathy. Higher rates of renal dysfunction have been reported in patients using TDF in conjunction with RTV-containing regimens.</td>
</tr>
<tr>
<td>TAF may be used if CrCl &gt;30 mL/min or if patient is on chronic hemodialysis (only studied with EVG/c/TAF/FTC). Consider avoiding ATV.</td>
<td></td>
<td></td>
<td>An adjusted dose of TDF can be used in patients with ESRD or in those who are on hemodialysis. Refer to Appendix B, Table 10 for specific dosing recommendations.</td>
</tr>
<tr>
<td>ART Options When ABC, TAF, or TDF Cannot be Used:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• DTG/3TC (if HIV RNA &lt;500,000 copies/mL and without HBV coinfection)</td>
<td></td>
<td></td>
<td>TAF has less impact on renal function and lower rates of proteinuria than TDF.</td>
</tr>
<tr>
<td>• DRV/r plus 3TC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• DRV/r plus RAL (if CD4 count &gt;200 cells/mm³ and HIV RNA &lt;100,000 copies/mL)</td>
<td></td>
<td></td>
<td>ATV has been associated with chronic kidney disease in some observational studies.</td>
</tr>
<tr>
<td><strong>Liver disease with cirrhosis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Some ARVs are contraindicated or may require dosage modification in patients with Child-Pugh class B or C disease.</td>
<td></td>
<td></td>
<td>ABC has not been associated with renal dysfunction.</td>
</tr>
<tr>
<td><strong>Osteoporosis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avoid TDF.a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABC may be used if patient is HLA-B*5701 negative. If HIV RNA is &gt;100,000 copies/mL, do not use ABC/3TC plus (EFV or ATV/r).</td>
<td></td>
<td></td>
<td>TDF is associated with decreases in BMD along with renal tubulopathy, urine phosphate wasting, and resultant osteomalacia. TAF and ABC are associated with smaller declines in BMD than TDF.</td>
</tr>
</tbody>
</table>
Table 7. Antiretroviral Regimen Considerations for 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>Psychiatric illnesses</td>
<td>Consider avoiding EFV- and RPV-based regimens.</td>
<td>EFV and RPV can exacerbate psychiatric symptoms and may be associated with suicidality.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Patients on INSTI-based regimens who have pre-existing psychiatric conditions should be closely monitored.</td>
<td>INSTIs have been associated with adverse neuropsychiatric effects in some retrospective cohort studies and case series.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Some ARVs are contraindicated, and some psychiatric medications need dose adjustments when coadministered with certain ARVs.</td>
<td>See the drug-drug interaction tables (Tables 21a, 21b, and 21d) for dosing recommendations when drugs used for psychiatric illnesses are used with certain ARVs.</td>
</tr>
<tr>
<td></td>
<td>HIV-associated dementia (HAD)</td>
<td>Avoid EFV-based regimens if possible.</td>
<td>The beneficial effects of ART on HAD-symptoms may be confounded by EFV-related neuropsychiatric effects.</td>
</tr>
<tr>
<td></td>
<td>Medication-assisted treatment for opioid use disorder</td>
<td>Opioid withdrawal may occur when EFV is initiated in patients who are on a stable dose of methadone. Clinical monitoring is recommended, as medications used to treat opioid dependence may need to be adjusted in some patients.</td>
<td>EFV reduces methadone concentrations and may lead to withdrawal symptoms. See the drug-drug interaction tables (Tables 21a, 21b, and 21d) for dosing recommendations.</td>
</tr>
<tr>
<td></td>
<td>Cardiac QTc interval prolongation</td>
<td>Consider avoiding 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>
<td>High EFV or RPV concentrations may cause QT prolongation.</td>
</tr>
<tr>
<td></td>
<td>High cardiac risk</td>
<td>Consider avoiding ABC- and LPV/r -based regimens. If a boosted PI is the desired option, an ATV-based regimen may have advantages over a DRV-based regimen. Refer to Hyperlipidemia below for regimens associated with more favorable lipid profiles.</td>
<td>An increased risk of CV events with ABC has been observed in some studies. Observational cohort studies reported an association between some PIs (DRV, IDV, FPV, and LPV/r) and an increased risk of CV events; this risk has not been seen with ATV (see text). Further study is needed. Certain ART regimens are associated with more favorable lipid profiles than other regimens, although evidence on whether this improves CV outcomes is lacking.</td>
</tr>
<tr>
<td></td>
<td>Hyperlipidemia</td>
<td>The Following ARV Drugs Have Been Associated with Dyslipidemia: • PI/r or PI/c • EFV • EVG/c BIC, DOR, DTG, RAL, and RPV have fewer lipid effects. TDF lowers lipids; therefore, switching from TDF to TAF is associated with increased lipids.</td>
<td>TDF has been associated with lower lipid levels than ABC or TAF.</td>
</tr>
<tr>
<td>Patient or Regimen Characteristics</td>
<td>Clinical Scenario</td>
<td>Consideration(s)</td>
<td>Rationale/Comments</td>
</tr>
<tr>
<td>------------------------------------</td>
<td>-------------------</td>
<td>------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>Presence of Other Conditions, continued</td>
<td>Patients with history of poor adherence to non-ARV medications or inconsistent engagement in care</td>
<td>Consider using regimens with a boosted PI or BIC or DTG.</td>
<td>These regimens have a high genetic barrier to resistance.</td>
</tr>
<tr>
<td></td>
<td>Pregnancy</td>
<td>Refer to Table 6b and the Perinatal Guidelines for further guidance on ARV use during pregnancy.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Patients of childbearing potential who are planning to become pregnant or who are sexually active and not using effective contraception</td>
<td>Refer to Table 6b for further guidance.</td>
<td></td>
</tr>
<tr>
<td>Presence of Coinfections</td>
<td>HBV infection</td>
<td>Use TDF or TAF, with FTC or 3TC If TDF and TAF Are Contraindicated: • For treatment of HBV, use FTC or 3TC with entecavir and a suppressive ART regimen (see HBV/HIV Coinfection).</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 that is active against HBV.</td>
</tr>
<tr>
<td></td>
<td>HCV treatment required</td>
<td>Refer to recommendations in HCV/HIV Coinfection, with special attention to potential interactions between ARV drugs and HCV drugs.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treating TB disease with rifamycin antibiotics (rifabutin, rifampin, and rifapentine)</td>
<td>Recommended regimens may require dose adjustment. See the drug-drug interaction tables (Tables 21a-e) and TB/HIV Coinfection for information on ARV use with rifamycin antibiotics.</td>
<td>Rifamycin antibiotics are inducers of CYP3A4 and UGT1A1 enzymes, causing significant decreases in concentrations of PIs, INSTIs, and RPV.</td>
</tr>
</tbody>
</table>

a TAF and TDF are two FDA-approved forms of TFV. TAF has fewer 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: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; BID = twice daily; BMD = bone mineral density; COBI = cobicistat; CD4 = CD4 T lymphocyte; CNS = central nervous system; CrCl = creatinine clearance; CV = cardiovascular; CYP = cytochrome P; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ESRD = end stage renal disease; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FDA = Food and Drug Administration; FPV = fosamprenavir; FTC = emtricitabine; HAD = HIV-associated dementia; HBV = hepatitis B virus; HCV = hepatitis C virus; HLA = human leukocyte antigen; IDV = indinavir; INSTI = integrase strand transfer inhibitor; LPV = lopinavir; LPV/r = lopinavir/ritonavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NTD = neural tube defect; PI = protease inhibitor; PI/c = cobicistat-boosted protease inhibitor; PI/r = ritonavir-boosted protease inhibitor RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; STR = single-tablet regimen; TAF = tenofovir alafenamide; TB = tuberculosis; TDF = tenofovir disoproxil fumarate; TFV = tenofovir; UGT = uridine diphosphate glucuronosyltransferase.
### Table 8a. Characteristics of Nucleoside Reverse Transcriptase Inhibitor Options Recommended for Antiretroviral Therapy-Naive Patients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>ABC/3TC</th>
<th>3TC&lt;sup&gt;a&lt;/sup&gt;</th>
<th>TDF/3TC</th>
<th>TAF/FTC</th>
<th>TDF/FTC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dosing Frequency</strong></td>
<td>Once daily</td>
<td>Once daily</td>
<td>Once daily</td>
<td>Once daily</td>
<td>Once daily</td>
</tr>
<tr>
<td><strong>Available Coformulations for ART-Naive Patients</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• ABC/3TC</td>
<td></td>
<td>DTG/3TC</td>
<td></td>
<td>3TC: No significant adverse effects</td>
<td></td>
</tr>
<tr>
<td>• DTG/ABC/3TC</td>
<td></td>
<td></td>
<td></td>
<td>FTCl: Skin discoloration</td>
<td></td>
</tr>
<tr>
<td><strong>Adverse Effects</strong></td>
<td>ABC:</td>
<td>TDF:</td>
<td>TAF:</td>
<td>TDF:</td>
<td></td>
</tr>
<tr>
<td>• HSR to ABC is associated with the presence of HLA-B*5701 allele.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Increase in CV events is associated with ABC use in some, but not all, cohort studies.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>3TC:</strong> No significant adverse effects</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Other Considerations</strong></td>
<td>ABC:</td>
<td>TDF:</td>
<td>TAF:</td>
<td>TDF:</td>
<td></td>
</tr>
<tr>
<td>• Perform HLA-B*5701 testing before initiating ABC; if result is positive, do not start ABC and add ABC to patient’s allergy list.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>3TC:</strong></td>
<td></td>
<td>TDF:</td>
<td>TAF:</td>
<td>TDF:</td>
<td></td>
</tr>
<tr>
<td>• Epivir HBV&lt;sup&gt;TM&lt;/sup&gt; is for the treatment of HBV and contains a different dose of 3TC than the formulation for ART. Thus, Epivir HBV&lt;sup&gt;TM&lt;/sup&gt; should not be used for HIV treatment.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Coadministration of 3TC with sorbitol-containing drugs decreases 3TC concentration and should be avoided.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

<sup>a</sup> 3TC is recommended for use with DTG in ART-naive persons, and with DRV/r if ABC, TDF, and TAF are not optimal. Otherwise, dual-NRTI backbones are recommended.

**Key:**
- 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; BIC = bبت/gravir; BMD = bone mineral density; CV = cardiovascular; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; HBV = hepatitis B virus; HLA = human leukocyte antigen; HSR = hypersensitivity reaction; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate
### Table 8b. Characteristics of Integrase Strand Transfer Inhibitors That Are Recommended for Antiretroviral Therapy-Naive Patients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>BIC</th>
<th>DTG</th>
<th>EVG</th>
<th>RAL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dosing Frequency</strong></td>
<td>Once daily</td>
<td><strong>Once Daily:</strong>&lt;br&gt;• In ART-naive or INSTI-naive persons&lt;br&gt;<strong>Twice Daily:</strong>&lt;br&gt;• If used with certain CYP3A4 and UGT1A1 inducers; or&lt;br&gt;• In INSTI-experienced persons with certain INSTI drug resistance mutations</td>
<td>Once daily; requires boosting with COBI</td>
<td>• 400 mg twice daily, or&lt;br&gt;• 1,200 mg (two 600-mg tablets) once daily</td>
</tr>
<tr>
<td><strong>STR Available for ART-Naive Patients</strong></td>
<td>BIC/TAF/FTC</td>
<td>DTG/ABC/3TC&lt;br&gt;• DTG/3TC</td>
<td>EVG/c/TAF/FTC&lt;br&gt;• EVG/c/TDF/FTC</td>
<td>No</td>
</tr>
<tr>
<td><strong>Available as a Single-Drug Tablet</strong></td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Approved for ART-Experienced Patients</strong></td>
<td>No</td>
<td>Yes, with twice-daily dosing for patients with certain INSTI drug resistance mutations</td>
<td>No, but sometimes used in combination with DRV and TAF/FTC as part of a simplification regimen in patients with resistance.</td>
<td>Yes, for patients with drug resistance mutations to RTV-boosted PIs or NNRTIs, but not to INSTIs</td>
</tr>
<tr>
<td><strong>Virologic Efficacy Against EVG- or RAL-Resistant HIV</strong></td>
<td><em>In vitro</em> data indicate activity, but clinical trial data are not available.</td>
<td>Yes, for some isolates; effective with DTG 50 mg twice-daily dose</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td><strong>Adverse Effects</strong></td>
<td>Nausea, diarrhea (GI disturbance greater with EVG/c), headache, insomnia. Depression and suicidality are rare, occurring primarily in patients with pre-existing psychiatric conditions.</td>
<td>Hypersensitivity, hepatotoxicity, ↑ CPK, myositis</td>
<td>↑ TG, ↑ LDL</td>
<td>↑ CPK, myopathy, hypersensitivity, SJS/TEN</td>
</tr>
<tr>
<td><strong>CYP3A4 Drug-Drug Interactions</strong></td>
<td>CYP3A4 substrate</td>
<td>CYP3A4 substrate (minor)</td>
<td>EVG is a CYP3A4 substrate; COBI is a CYP3A4 inhibitor</td>
<td>No</td>
</tr>
<tr>
<td><strong>Chelation with Polyvalent Cation Supplements and Antacids</strong></td>
<td>Oral absorption of all INSTIs may be reduced by polyvalent cations. See Table 21d for recommendations regarding dosing separation of INSTIs and these drugs.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Other Key Potential Drug Interactions</strong></td>
<td>UGT1A1 substrate, OCT2 and MATE1 inhibitor</td>
<td>P-gp substrate, UGT1A1 substrate</td>
<td>EVG is a UGT1A1 substrate; COBI is a P-gp inhibitor.</td>
<td>UGT1A1 substrate</td>
</tr>
</tbody>
</table>

*Key:* 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; BIC = bictegravir; BID = twice daily; COBI = cobicistat; CPK = creatine phosphokinase; CYP = cytochrome P; DRV = darunavir; DTG = dolutegravir; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; GI = gastrointestinal; INSTI = integrase strand transfer inhibitor; LDL = low density lipoprotein; MATE = multidrug and toxic compound extrusion; NNR1 = non-nucleoside reverse transcriptase inhibitor; NTD = neural tube defect; OAT = organic cation transporter; P-gp = p-glycoprotein; PI = protease inhibitor; PI/r = ritonavir-boosted protease inhibitor; RAL = raltegravir; SJS/TEN = Stevens Johnson Syndrome/toxic epidermal necrolysis; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TG = triglyceride; UGT = uridine diphosphate glucuronosyltransferase
Table 8c. Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors that are Recommended for Antiretroviral Therapy-Naive Patients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>DOR</th>
<th>EFV</th>
<th>RPV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dosing Frequency</strong></td>
<td>Once daily</td>
<td>Once daily</td>
<td>Once daily</td>
</tr>
<tr>
<td><strong>Food Requirement</strong></td>
<td>With or without food</td>
<td>On an empty stomach</td>
<td>With a meal</td>
</tr>
<tr>
<td><strong>STR Available for ART-Naive Patients</strong></td>
<td>DOR/TDF/3TC</td>
<td>• EFV 600 mg/TDF/FTC</td>
<td>• RPV/TAF/FTC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• EFV 600 mg/TDF/3TC</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• EFV 400 mg/TDF/3TC</td>
<td></td>
</tr>
<tr>
<td><strong>Available as a Single-Drug Tablet</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Adverse Effects</strong></td>
<td>Generally well tolerated</td>
<td>• CNS side effects, including dizziness, abnormal dreams, headache, depression, suicidality, insomnia, somnolence</td>
<td>• Depression, headache</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Skin rash</td>
<td>• Skin rash</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>QTc prolongation</strong></td>
<td><strong>QTc prolongation</strong></td>
</tr>
<tr>
<td><strong>CYP3A4 Drug-Drug Interactions</strong></td>
<td>CYP3A4 substrate</td>
<td>CYP3A4 substrate, mixed inducer/inhibitor</td>
<td>CYP3A4 substrate</td>
</tr>
<tr>
<td><strong>Other Significant Drug Interactions</strong></td>
<td>None</td>
<td>CYP2B6 and 2C19 inducer</td>
<td>RPV oral absorption is reduced with increased gastric pH. Use of RPV with PPIs is not recommended; see Drug-Drug Interactions for dosing recommendations when RPV is coadministered with H2 blocker or antacids.</td>
</tr>
</tbody>
</table>

Key: 3TC = lamivudine; CNS = central nervous system; CYP = cytochrome P; DOR = doravirine; EFV = efavirenz; FTC = emtricitabine; H2 = histamine 2; PPI = proton pump inhibitor; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate
### Table 8d. Characteristics of Protease Inhibitor Options that are Recommended for Antiretroviral Therapy-Naive Patients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>ATV</th>
<th>DRV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosing Frequency</td>
<td>Once daily</td>
<td>• Once daily for PI-naive patients</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DRV should only be used with a PK booster (i.e., RTV or COBI).</td>
</tr>
<tr>
<td>PK Boosting</td>
<td>PK-boosting with RTV or COBI is generally recommended. Unboosted ATV is also FDA-approved for ART-naive patients.</td>
<td>• ATV/c</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• DRV/c</td>
</tr>
<tr>
<td>Available as a Single-Drug Tablet</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Adverse Effects</td>
<td>• Jaundice</td>
<td>• Skin rash</td>
</tr>
<tr>
<td></td>
<td>• Indirect hyperbilirubinemia</td>
<td>• Increase in serum transaminases</td>
</tr>
<tr>
<td></td>
<td>• Cholelithiasis</td>
<td>• Hyperlipidemia</td>
</tr>
<tr>
<td></td>
<td>• Nephrolithiasis</td>
<td>• A higher cardiovascular risk was reported in participants taking DRV-based regimens than in those taking ATV-based regimens in an observational cohort study.</td>
</tr>
<tr>
<td></td>
<td>• PR prolongation</td>
<td></td>
</tr>
<tr>
<td>CYP3A4 Drug-Drug Interactions</td>
<td>CYP3A4 substrate, inhibitor</td>
<td>CYP3A4A substrate, inhibitor</td>
</tr>
<tr>
<td>Other Significant Drug Interactions</td>
<td>ATV absorption is reduced when ATV is given with acid-lowering therapies. See Table 21a for ATV dosing recommendations when the drug is coadministered with acid-lowering agents.</td>
<td>N/A</td>
</tr>
</tbody>
</table>

**Key:** ART = antiretroviral therapy; ATV = atazanavir; ATV/c = atazanavir/cobicistat; COBI = cobicistat; CYP = cytochrome P; DRV = darunavir; DRV/c = darunavir/cobicistat; FDA = Food and Drug Administration; FTC = emtricitabine; N/A = not applicable; PI = protease inhibitor; PK = pharmacokinetic; RTV = ritonavir; TAF = tenofovir alafenamide
### Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy (continued)

<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>Dual-NRTI Regimens</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABC/3TC</td>
<td></td>
<td>• Coformulated with DTG</td>
<td>• May cause life-threatening HSRs in patients who test positive for the HLA-B<em>5701 allele. As a result, HLA-B</em>5701 testing is required before use.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Generic formulations are available for ABC/3TC, ABC, and 3TC.</td>
<td>• 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.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• ABC use has been associated with CV disease and cardiac events in some, but not all, observational studies.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• May cause life-threatening HSRs in patients who test positive for the HLA-B<em>5701 allele. As a result, HLA-B</em>5701 testing is required before use.</td>
<td></td>
</tr>
<tr>
<td>TAF/FTC</td>
<td></td>
<td>• Coformulated with BIC, DRV/c, EVG/c, or RPV</td>
<td>• TDF is associated with lower lipid levels than TAF, perhaps because TDF results in higher plasma levels of tenofovir, which lowers lipids.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Active against HBV; a recommended dual-NRTI option for patients with HBV/HIV coinfection</td>
<td>• Not recommended in pregnancy.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Smaller decline in renal function, less proteinuria, and smaller reductions in BMD than TDF/FTC</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Approved for patients with eGFR ≥30 mL/min</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Can be used in patients with eGFR &lt;30 mL/min and on chronic hemodialysis</td>
<td></td>
</tr>
<tr>
<td>TDF/3TC</td>
<td></td>
<td>• Coformulated with DOR</td>
<td>• Renal toxicity, including proximal tubulopathy and acute or chronic renal insufficiency, especially when combined with pharmacologic boosters.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Generic formulations are available for TDF, 3TC, TDF/3TC, and EFV/TDF/3TC.</td>
<td>• Osteomalacia has been reported as a consequence of proximal tubulopathy.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Long-term clinical experience</td>
<td>• Decreased BMD has been associated with use of TDF, especially when combined with pharmacologic boosters.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Active against HBV</td>
<td></td>
</tr>
<tr>
<td>TDF/FTC</td>
<td></td>
<td>• Coformulated with EFV, EVG/c, and RPV as STRs</td>
<td>• Renal toxicity, including proximal tubulopathy and acute or chronic renal insufficiency, especially when combined with pharmacologic boosters.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Active against HBV; a recommended dual-NRTI option for patients with HIV/HBV coinfection</td>
<td>• Osteomalacia has been reported as a consequence of proximal tubulopathy.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Better virologic responses than ABC/3TC in patients with baseline viral loads ≥100,000 copies/mL when combined with ATV/r or EFV</td>
<td>• Decreased BMD has been associated with use of TDF, especially when combined with pharmacologic boosters.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Associated with lower lipid levels than ABC or TAF</td>
<td></td>
</tr>
</tbody>
</table>

Note: All drugs within an ARV class are listed in alphabetical order.
### Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy

<table>
<thead>
<tr>
<th>ARV Class</th>
<th>ARV Agent(s)</th>
<th>Advantage(s)</th>
<th>Disadvantage(s)</th>
</tr>
</thead>
</table>
| Single NRTI | 3TC          | • Coformulated with DTG as STR  
• Avoids potential toxicities associated with TDF, TAF, ABC                   | • DTG/3TC is not recommended for individuals with HIV RNA >500,000 copies/mL, HBV co-infection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available. |
| INSTI       | BIC          | • Coformulated with TAF/FTC  
• Higher barrier to resistance than EVG and RAL  
• No food requirement                                                                 | • See Table 6b for considerations related to prescribing an INSTI-based regimen to people of childbearing potential.  
• Oral absorption of BIC can be reduced by simultaneous administration with drugs or supplements containing polyvalent cations (e.g., Al-, Ca-, or Mg-containing antacids or supplements, or multivitamin tablets with minerals). See dosing recommendations in Table 21d.  
• Should not be used in pregnancy because of lack of data and coformulation with TAF  
• See discussion in text regarding weight gain related to INSTIs. |
| DTG         |              | • Higher barrier to resistance than EVG or RAL  
• Coformulated with ABC/3TC and 3TC  
• No food requirement  
• Minimal CYP3A4 interactions  
• Favorable lipid profile                                                                 | • Data from Botswana suggest that DTG exposure during conception may be associated with risk of NTDs in the infant (0.3% vs. 0.1% with non-DTG ARV drugs).  
• See Table 6b for considerations related to prescribing an INSTI-based regimen for a person of childbearing potential.  
• 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 21d.  
• Inhibits renal tubular secretion of Cr and can increase serum Cr without affecting glomerular function.  
• UGT1A1 substrate; potential for drug interactions (see Table 21d).  
• Depression and suicidal ideation (rare; usually in patients with pre-existing psychiatric conditions).  
• See discussion in text regarding weight gain related to INSTIs. |
### Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy (page 3 of 5)

<table>
<thead>
<tr>
<th>ARV Class</th>
<th>ARV Agent(s)</th>
<th>Advantage(s)</th>
<th>Disadvantage(s)</th>
</tr>
</thead>
</table>
| INSTI,    | EVG/c        | - Coformulated with TDF/FTC or TAF/FTC  
- Compared with ATV/r, EVG/c causes smaller increases in total and LDL cholesterol.  
- EVG/c/TAF/FTC can be used in patients on chronic hemodialysis. | • See Table 6b for considerations related to prescribing an INSTI-based regimen for a person of childbearing potential.  
• 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 21d.  
• COBI inhibits active tubular secretion of Cr and can increase serum Cr without affecting renal glomerular function.  
• Has a lower barrier to resistance than boosted PI-, BIC-, or DTG-based regimens.  
• Food requirement.  
• Depression and suicidal ideation (rare; usually in patients with pre-existing psychiatric conditions).  
• Should not be used in pregnancy because of low drug exposure.  
• See discussion in text regarding weight gain related to INSTIs. |
| RAL------- |              | - Compared to other INSTIs, has longest post-marketing experience  
- No food requirement  
- No CYP3A4 interactions  
- Favorable lipid profile |                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                    |
| NNRTI     | DOR          | - Coformulated with TDF/3TC  
- Compared to EFV, fewer CNS side effects  
- No food requirement  
- Favorable lipid profile | • See Table 6b for considerations related to prescribing an INSTI-based regimen for a person of childbearing potential.  
• Has a lower barrier to resistance than boosted PI-, BIC-, 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 FDC 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 21d.  
• UGT1A1 substrate; potential for drug interactions (see Table 21d).  
• Depression and suicidal ideation (rare; usually in patients with pre-existing psychiatric conditions).  
• See discussion in text regarding weight gain related to INSTIs.  
• Potential for CYP450 drug interactions (see Tables 21b, 22a and 22b).  
• Treatment-emergent DOR resistance mutations may confer resistance to certain NNRTIs. |

**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 7/3/2020
**Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy** (page 4 of 5)

<table>
<thead>
<tr>
<th>ARV Class</th>
<th>ARV Agent(s)</th>
<th>Advantage(s)</th>
<th>Disadvantage(s)</th>
</tr>
</thead>
</table>
| NNRTI, continued | EFV | • EFV 600 mg is coformulated with TDF/FTC and TDF/3TC.  
• EFV 400 mg is coformulated with TDF/3TC.  
• EFV 600-mg dose has long-term clinical experience and EFV-based regimens (except for EFV plus ABC/3TC) have well-documented efficacy in patients with high HIV RNA.  
• EFV 400 mg has fewer CNS side effects than EFV 600 mg.  
• EFV 600 mg can be given with rifamycin antibiotics (rifampin, rifabutin, or rifapentine). | • Short- and long-term neuropsychiatric (CNS) side effects, including depression and, in some studies, suicidality and catatonia. Late onset ataxia and encephalopathy have also been reported.  
• Periodic screening for depression and suicidality is recommended in people with HIV who are taking a regimen that includes EFV.  
• Dyslipidemia  
• Rash  
• QTc interval prolongation; consider using an alternative to EFV in patients taking medications with known risk of causing Torsades de Pointes or in those at higher risk of Torsades de Pointes.  
• Transmitted resistance is 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 21b and 22a).  
• 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 sizes 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 counts <200 cells/mm³ because of higher rate of virologic failure in these patients.  
• Depression and suicidality  
• QTc interval prolongation; consider using an alternative to RPV in patients taking medications with known risk of causing Torsades de Pointes or in those at higher risk of Torsades de Pointes.  
• Rash  
• Transmitted resistance is more common than with PIs and INSTIs.  
• More NNRTI-, TDF-, and 3TC-associated mutations at virologic failure than with regimens that contain EFV and 2 NRTIs.  
• Potential for CYP450 drug interactions (see Tables 21b and 22a).  
• Meal requirement (>390 kcal)  
• Requires acid for adequate absorption.  
• Contraindicated with PPIs.  
• Use with H2 antagonists or antacids with caution (see Table 21a for detailed dosing information). |
| PIs | ATV/c or ATV/r | • Higher barrier to resistance than NNRTIs, EGV, and RAL  
• PI resistance at the time of treatment failure is 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; this risk has not been seen with ATV. Further study is needed. See text for discussion.  
• Individual ATV and RTV components are available as generics. | • Commonly causes indirect hyperbilirubinemia, which may manifest as scleral icterus or jaundice.  
• Food requirement  
• Absorption depends on food and low gastric pH (see Table 21a for interactions with H2 antagonists, antacids, and PPIs).  
• Nephrolithiasis, cholelithiasis, nephrotoxicity  
• GI adverse effects  
• CYP3A4 inhibitors and substrates: potential for drug interactions (see Table 21a). |
Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy  (page 5 of 5)

<table>
<thead>
<tr>
<th>ARV Class</th>
<th>ARV Agent(s)</th>
<th>Advantage(s)</th>
<th>Disadvantage(s)</th>
</tr>
</thead>
</table>
| PIs, continued | ATV/c | Coformulated tablet | • 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 <70 mL/min.  
• COBI (like RTV) is a potent CYP3A4 inhibitor, which can result in significant interactions with CYP3A substrates.  
• COBI is not recommended in pregnancy because of low drug levels. |
|            | Specific considerations |            |                  |
|            | ATV/c |              |                  |
|            | ATV/r |              |                  |
|            | DRV/c or DRV/r | • Higher barrier to resistance than NNRTIs, EVG, and RAL  
• PI resistance at the time of treatment failure is uncommon with PK-enhanced PIs. | • Skin rash  
• Food requirement  
• GI adverse effects  
• CYP3A4 inhibitors and substrates: potential for drug interactions (see Table 21a).  
• Increased CV risk reported in one observational cohort study.  
• Hepatotoxicity has been reported, especially in those with pre-existing liver disease. |
|            | DRV/c Specific considerations | • Coformulated as DRV/c and DRV/c/TAF/FTC | • 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 <70 mL/min.  
• COBI (like RTV) is a potent CYP3A4 inhibitor, which can result in significant interactions with CYP3A substrates.  
• COBI is not recommended in pregnancy because of low drug levels. |

Key: 3TC = lamivudine; ABC = abacavir; Al = aluminum; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; BMD = bone mineral density; Ca = calcium; CD4 = CD4 T lymphocyte; CNS = central nervous system; COBI = cobicistat; Cr = creatinine; CrCl = creatinine clearance; CV = cardiovascular; CYP = cytochrome P; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; eGFR = estimated glomerular filtration rate; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FDC = fixed-dose combination; 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/r = lopinavir/ritonavir; Mg = magnesium; MI = myocardial infarction; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NTD = neural tube defect; PI = protease inhibitor; PK = pharmacokinetic; PPI = proton pump inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SJS = Stevens-Johnson syndrome; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TEN = toxic epidermal necrosis; UGT = uridine diphosphate glucuronosyltransferase
### Table 10. 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 plus TDF As quadruple-NRTI combination regimen</td>
<td>• Inferior virologic efficacy</td>
</tr>
<tr>
<td>d4T plus 3TC</td>
<td>• Significant toxicities (including lipoatrophy, peripheral neuropathy) and hyperlactatemia (including symptomatic and life-threatening lactic acidosis, hepatic steatosis, and pancreatitis)</td>
</tr>
<tr>
<td>d4T plus 3TC (or FTC)</td>
<td>• Inferior virologic efficacy&lt;br&gt;• Limited clinical trial experience in ART-naive patients&lt;br&gt;• ddi toxicities, such as pancreatitis and peripheral neuropathy</td>
</tr>
<tr>
<td>ddI plus TDF</td>
<td>• High rate of early virologic failure&lt;br&gt;• Rapid selection of resistance mutations&lt;br&gt;• Potential for immunologic nonresponse/CD4 cell decline&lt;br&gt;• Increased ddI drug exposure and toxicities</td>
</tr>
<tr>
<td>ZDV/3TC</td>
<td>• 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</td>
</tr>
<tr>
<td><strong>NNRTIs</strong></td>
<td></td>
</tr>
<tr>
<td>DLV</td>
<td>• Inferior virologic efficacy&lt;br&gt;• Inconvenient (three times daily) dosing</td>
</tr>
<tr>
<td>ETR</td>
<td>• Insufficient data in ART-naive patients</td>
</tr>
<tr>
<td>NVP</td>
<td>• Associated with serious and potentially fatal toxicity (hepatic events and severe rash, including SJS and TEN)&lt;br&gt;• When compared to EFV, NVP did not meet noninferiority criteria</td>
</tr>
<tr>
<td><strong>PIs</strong></td>
<td></td>
</tr>
<tr>
<td>ATV (Unboosted)</td>
<td>• Less potent than boosted ATV</td>
</tr>
<tr>
<td>DRV (Unboosted)</td>
<td>• Use without RTV or COBI has not been studied</td>
</tr>
<tr>
<td>FPV (Unboosted)</td>
<td>• Virologic failure with unboosted FPV-based regimen may result in selection of mutations that confer resistance to FPV and DRV&lt;br&gt;• Less clinical trial data for FPV/r than for other RTV-boosted PIs</td>
</tr>
<tr>
<td>or FPV/r</td>
<td></td>
</tr>
<tr>
<td>IDV (Unboosted)</td>
<td>• Inconvenient dosing (3 times daily with meal restrictions)&lt;br&gt;• Fluid requirement&lt;br&gt;• IDV toxicities, such as nephrolithiasis and crystalluria</td>
</tr>
<tr>
<td>IDV/r</td>
<td>• Fluid requirement&lt;br&gt;• IDV toxicities, such as nephrolithiasis and crystalluria</td>
</tr>
<tr>
<td>LPV/r</td>
<td>• Higher pill burden than other PI-based regimens&lt;br&gt;• Higher RTV dose than other PI-based regimens&lt;br&gt;• GI intolerance</td>
</tr>
<tr>
<td>NFV</td>
<td>• Inferior virologic efficacy&lt;br&gt;• Diarrhea</td>
</tr>
<tr>
<td>RTV as sole PI</td>
<td>• High pill burden&lt;br&gt;• GI intolerance&lt;br&gt;• Metabolic toxicity</td>
</tr>
</tbody>
</table>
Table 10. Antiretroviral Components or Regimens Not Recommended as Initial Therapy (page 2 of 2)

<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</td>
</tr>
<tr>
<td></td>
<td>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</td>
</tr>
<tr>
<td></td>
<td>RTV-boosted PIs</td>
</tr>
<tr>
<td></td>
<td>• Higher dose of RTV required for boosting</td>
</tr>
<tr>
<td></td>
<td>than other RTV-boosted PIs</td>
</tr>
<tr>
<td><strong>Entry Inhibitors</strong></td>
<td></td>
</tr>
<tr>
<td>T-20</td>
<td>• Only studied in patients with virologic</td>
</tr>
<tr>
<td>Fusion Inhibitor</td>
<td>failure</td>
</tr>
<tr>
<td></td>
<td>• Twice-daily subcutaneous injections</td>
</tr>
<tr>
<td></td>
<td>• High rate of injection site reactions</td>
</tr>
<tr>
<td>IBA</td>
<td>• Only studied in a very small number of</td>
</tr>
<tr>
<td>CD4 Post-Attachment Inhibitor</td>
<td>patients with virologic failure</td>
</tr>
<tr>
<td></td>
<td>• Requires IV therapy</td>
</tr>
<tr>
<td></td>
<td>• High cost</td>
</tr>
<tr>
<td>MVC</td>
<td>• Requires testing for CCR5 tropism before</td>
</tr>
<tr>
<td>CCR5 Antagonist</td>
<td>initiation of therapy</td>
</tr>
<tr>
<td></td>
<td>• No virologic benefit when compared with</td>
</tr>
<tr>
<td></td>
<td>other recommended regimens</td>
</tr>
<tr>
<td></td>
<td>• Requires twice-daily dosing</td>
</tr>
</tbody>
</table>

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; CD4 = CD4 T lymphocyte; COBI = cobicistat; d4T = stavudine; ddl = didanosine; DLV = delavirdine; DRV = darunavir; ECG = electrocardiogram; EFV = efavirenz; ETR = etravirine; FPV = fosamprenavir; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; GI = gastrointestinal; IBA = ibalizumab; IDV = indinavir; IDV/r = indinavir/ritonavir; IV = intravenous; LPV = lopinavir; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NFV = nevirapine; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; RTV = ritonavir; SJS = Stevens Johnson Syndrome; SQV = saquinavir; SQV/r = saquinavir/ritonavir; T-20 = enfuvirtide; TDF = tenofovir disoproxil fumarate; TEN = toxic epidermal necrolysis; TPV = tipranavir; TPV/r = tipranavir/ritonavir; ZDV = zidovudine
Table 11. Antiretroviral Options for Patients with Virologic Failure

Designing a new regimen for patients who are experiencing treatment failure should always be guided by ARV history and results from current and past resistance testing. This table summarizes the text above and displays the most common or likely clinical scenarios seen in patients with virologic failure. 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. It is also crucial to provide continuous adherence support to all patients before and after regimen changes.

<table>
<thead>
<tr>
<th>Clinical Scenario</th>
<th>Type of Failing Regimen</th>
<th>Resistance Considerations</th>
<th>New Regimen Options&lt;sup&gt;a,b&lt;/sup&gt;</th>
<th>Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Regimen Failure</td>
<td>NNRTI plus two NRTIs</td>
<td>Most likely resistant to NNRTI +/- 3TC or FTC (i.e., NNRTI mutations +/- M184V/I). Additional NRTI mutations may also be present.</td>
<td>Boosted PI plus two NRTIs (at least one active) (AIII); or DTG&lt;sup&gt;d&lt;/sup&gt; plus two NRTIs (at least one active) (AI); or Boosted PI plus INSTI (AIII)</td>
<td>Resuppression</td>
</tr>
<tr>
<td></td>
<td>Boosted PI plus two NRTIs</td>
<td>Most likely no resistance, or resistance only to 3TC or FTC (i.e., M184V/I, without resistance to other NRTIs)&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Continue same regimen (AI); or Another boosted PI plus two NRTIs (at least one active) (AII); or INSTI plus two NRTIs (at least one active; if only one of the NRTIs is fully active, or if adherence is a concern, DTG&lt;sup&gt;d&lt;/sup&gt; is preferred over other INSTIs) (AIII); or Another boosted PI plus INSTI (BIII)</td>
<td>Resuppression</td>
</tr>
<tr>
<td></td>
<td>INSTI plus two NRTIs</td>
<td>No INSTI resistance (can have 3TC or FTC resistance, i.e., only M184V/I, usually without resistance to other NRTIs)&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Boosted PI plus two NRTIs (at least one active) (AIII); or DTG&lt;sup&gt;d&lt;/sup&gt; plus two NRTIs (at least one active) (AIII); or Boosted PI plus INSTI (BIII)</td>
<td>Resuppression</td>
</tr>
<tr>
<td></td>
<td>EVG or RAL +/- 3TC or FTC resistance</td>
<td>Resistance to first-line BIC or DTG is rare.</td>
<td>Boosted PI plus two NRTIs (at least one active) (AIII); or DTG&lt;sup&gt;es&lt;/sup&gt; twice daily (if HIV is sensitive to DTG) plus two active NRTIs (AIII); or DTG&lt;sup&gt;es&lt;/sup&gt; twice daily (if HIV is sensitive to DTG) plus a boosted PI (AIII) BIC has not been studied in this setting and cannot be recommended.</td>
<td>Resuppression</td>
</tr>
<tr>
<td>Second Regimen Failure</td>
<td>Drug resistance with active treatment options</td>
<td>Use past and current genotypic +/- phenotypic resistance testing and ART history when designing new regimen.</td>
<td>At least two, and preferably three, fully active agents (AI) Partially active drugs may be used when no other options are available. Consider using an ARV drug with a different mechanism of action.</td>
<td>Resuppression</td>
</tr>
</tbody>
</table>

<sup>a</sup>DTG<sub>d</sub> is preferred over other INSTIs when possible.  
<sup>b</sup>EVG or RAL must be used in combination with at least two active drugs.  
<sup>c</sup>Additional NRTI mutations may also be present.  
<sup>d</sup>BIC has not been studied in this setting and cannot be recommended.
Table 11. Antiretroviral Options for Patients with Virologic Failure, continued

<table>
<thead>
<tr>
<th>Clinical Scenario</th>
<th>Type of Failing Regimen</th>
<th>Resistance Considerations</th>
<th>New Regimen Options&lt;sup&gt;a,b&lt;/sup&gt;</th>
<th>Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Second Regimen Failure and Beyond, continued</strong></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 when use of MVC 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 test results. Consider using an ARV drug with a different mechanism of action. Consider enrollment into clinical trials or expanded access programs for investigational agents, if available. Discontinuation of ARV drugs is not recommended.</td>
<td>Resuppression, if possible; otherwise, keeping viral load as low as possible and CD4 count as high as possible.</td>
</tr>
</tbody>
</table>

<sup>a</sup> There are insufficient data to provide a recommendation for the continuation of 3TC or FTC in the presence of M184V/I.

<sup>b</sup> When switching an ARV regimen in a patient with HBV/HIV coinfection, ARV drugs that are active against HBV should be continued as part of the new regimen. Discontinuation of these drugs may lead to the reactivation of HBV, which may result in serious hepatocellular damage.

<sup>c</sup> If other NRTI resistance mutations are present, use resistance test results to guide NRTI usage in the new regimen.

<sup>d</sup> Data from an observational study in Botswana suggest that there is an increased risk of NTDs in infants born to individuals who were receiving DTG at the time of conception; however, the risk of these defects is still low. Please refer to the discussion in the text and in Table 6b before prescribing DTG in persons of childbearing potential.

<sup>e</sup> Response to DTG depends on the type and number of INSTI mutations.

**Key:** 3TC = lamivudine; ART = antiretroviral therapy; ARV = antiretroviral; BIC = bictegravir; CD4 = CD4 T lymphocyte; DRV = darunavir; DTG = dolutegravir; EVG = elvitegravir; FTC = emtricitabine; HBV = hepatitis B virus; INSTI = integrase strand transfer inhibitor; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NTD = neural tube defect; PI = protease inhibitor; RAL = raltegravir

---

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 7/3/2020
Table 12. Identifying, Diagnosing, and Treating Acute and Recent HIV Infection

Suspicions of Acute HIV Infection:

- Health care providers should consider the possibility of acute HIV infection in individuals with the signs, symptoms, or laboratory findings described below, and recent (within 2 to 6 weeks) high risk of exposure to HIV.\(^a\)
- Signs, symptoms, or laboratory findings of acute HIV 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, and transaminase elevation.
- High-risk exposures include sexual contact with a person who has HIV or a person at risk of HIV infection; sharing needles and syringes to inject drugs, as well as equipment used to prepare drugs for injection; or any exposure in which an individual's mucous membranes or any breaks in the skin come in contact with bodily fluid that potentially carries HIV.

Differential Diagnosis:

- The differential diagnosis of acute HIV infection may include but is not limited to viral illnesses such as EBV and non-EBV (e.g., CMV) infectious mononucleosis syndromes, influenza, viral hepatitis, streptococcal infection, or syphilis. Diagnosis of any STI should prompt HIV testing and consideration of acute or early HIV infection.

Testing to Diagnose/Confirm Acute HIV Infection:

- Acute HIV infection is defined as detectable HIV RNA or p24 antigen (the specific antigen used in currently available HIV-1/2 Ag/Ab combination assays) in the setting of a negative or indeterminate HIV 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 antibody test result in a person with a reactive Ag/Ab test result or in whom acute HIV infection is suspected requires plasma HIV RNA testing to diagnose acute HIV infection.
- A positive result on a quantitative or qualitative plasma HIV RNA test in the setting of a negative or indeterminate antibody test result indicates that acute HIV infection is highly likely. In this case, the diagnosis of HIV infection should be later confirmed by subsequent documentation of HIV infection seroconversion.

ART After Diagnosis of Early HIV Infection:

- ART should be initiated as soon as possible after HIV diagnosis (AII).
- ART is recommended for all individuals with HIV, including those with early\(^b\) HIV infection (AI). ART should be initiated as soon as possible after HIV diagnosis (AII).
- Once initiated, the goals of ART are to achieve sustained plasma virologic suppression and to prevent HIV transmission (AII).
- All individuals of childbearing potential who receive a diagnosis of early HIV infection should have a pregnancy test (AIII).
- Pregnant individuals with early HIV infection should begin ART as soon as possible for their own health and to prevent perinatal transmission of HIV (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 ART should be initiated as soon as possible, often before resistance test results are available. If resistance is subsequently identified, treatment should be modified as needed.
- ART can be initiated before the results of drug resistance testing are known. In this setting, one of the following ART regimens is recommended (AII):
  - DTG with (TAF or TDF)\(^b\) plus (FTC or 3TC)
  - BIC/TAF/FTC
  - Boosted DRV with (TAF or TDF)\(^b\) plus (FTC or 3TC)
- Pregnancy testing should be performed in individuals of childbearing potential before initiation of ART (AIII).
- Preliminary data from Botswana suggested that there is an increased risk of NTDs (0.9%) in infants born to women who were receiving DTG at the time of conception.\(^{42}\) Follow-up data, however, showed that the prevalence of NTDs in association with DTG exposure at conception is lower (0.3%), but still slightly higher than with non-DTG containing ARV regimens (0.1%).\(^{44,47}\) Before initiating an INSTI-based regimen in a person of childbearing potential, clinicians should review Table 6b for information to consider when choosing an ART regimen.

Key: 3TC = lamivudine; Ag/Ab = antigen/antibody; ART = antiretroviral therapy; ARV = antiretroviral; BIC = bictegravir; CMV = cytomegalovirus; DRV = darunavir; DTG = dolutegravir; EBV = Epstein-Barr virus; FTC = emtricitabine; INSTI = integrase strand transfer inhibitor; NTD = neural tube defect; STI = sexually transmitted infection; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TFV = tenofovir

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

Downloaded from https://aidsinfo.nih.gov/guidelines on 7/3/2020
### Table 13. Medications for Treatment of Substance Use Disorders

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose and Recommendations</th>
<th>Potential Interaction with ARV Drugs</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alcohol Use Disorder</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acamprosate</td>
<td>666 mg PO three times a day or 333 mg PO three times a day for patients with CrCl 30–50 mL/min</td>
<td>No significant interaction with ARV drugs expected.</td>
<td>Contraindicated in patients with CrCl &lt;30 mL/min.</td>
</tr>
<tr>
<td>Disulfiram</td>
<td>250 mg PO once daily</td>
<td>Use with caution when prescribing an ARV oral solution that contains ethanol and/or propylene glycol (e.g., FPV, LPV/r, RTV).</td>
<td>Counsel patients regarding disulfiram reaction when taken with alcohol; symptoms for the reaction may include flushing, tachycardia, nausea, vomiting, or hypotension.</td>
</tr>
<tr>
<td>Naltrexone</td>
<td>50–100 mg PO once daily Depot formulation is a fixed-dose monthly injection.</td>
<td>No significant interaction with ARV drugs expected.</td>
<td>Has the greatest efficacy of all FDA-approved medications for alcohol use disorder.</td>
</tr>
<tr>
<td><strong>Opioid Use Disorder</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>Individualize buprenorphine dosing based on a patient's opioid use. The dose range is 4–24 mg sublingually. Dosing is once daily or twice daily.</td>
<td>Potential interaction with ARV drugs that are CYP inhibitors or inducers. See Drug-Drug Interactions for further recommendations.</td>
<td>Buprenorphine has 90% first pass hepatic metabolism. Verify that the patient is using the appropriate technique for sublingual administration before adjusting the dose, as improper administration will result in poor absorption and low drug levels.</td>
</tr>
<tr>
<td>Methadone</td>
<td>Individualize dose. Patients who receive higher doses (&gt;100 mg) are more likely to remain in treatment.</td>
<td>Potential interaction with ARV drugs that are CYP inhibitors or inducers. See Drug-Drug Interactions for further recommendations.</td>
<td>QTc prolongation is a concern at higher doses. Methadone can only be prescribed for OUD by a licensed OTP.</td>
</tr>
<tr>
<td>Naltrexone</td>
<td>50–100 mg PO once daily Depot formulation is a fixed-dose monthly injection.</td>
<td>No significant interaction with ARV drugs expected.</td>
<td>Longer time of continuous abstinence in those who received depot formulation naltrexone compared to placebo after transition from prison to community.</td>
</tr>
<tr>
<td><strong>Nicotine Use Disorder</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nicotine Replacement Therapy</td>
<td>There are a wide variety of FDA-approved nicotine replacement products. All formulations are effective.</td>
<td>No significant interaction with ARV drugs expected.</td>
<td>Work with the patient to identify the route of delivery that the patient will use and find most helpful.</td>
</tr>
<tr>
<td>Bupropion</td>
<td>Start at 150 mg PO daily for three days, then increase to either 150 mg twice daily or 300 mg once daily (only use formulations that are approved for once daily dosing). Requires dose adjustment in patients with CrCl &lt;30 mL/min.</td>
<td>Concentration may be reduced when used with ARV drugs that are CYP2D6 inducers. See Drug-Drug Interactions for further recommendations.</td>
<td>Tobacco quit date should ideally be 1 week after starting therapy.</td>
</tr>
<tr>
<td>Varenicline</td>
<td>Titrate dose based on tolerability until desired effect is achieved. The goal is to reach a dose of 1 mg PO twice daily. Requires dose adjustment in patients with CrCl &lt;30 mL/min.</td>
<td>No significant interaction with ARV drugs expected.</td>
<td>Tobacco quit date should ideally be 1 week after starting therapy.</td>
</tr>
</tbody>
</table>

**Key:** ARV = antiretroviral; CrCl = creatinine clearance; CYP = cytochrome P; FDA = Food and Drug Administration; FPV = fosamprenavir; LPV/r = lopinavir/ritonavir; OUD = opioid use disorder; OTP = opioid treatment program; PO = orally; RTV = ritonavir; SR = sustained release
### Table 14. Potential Interactions Between the Drugs Used in Gender-Affirming Hormone Therapy and Antiretroviral Drugs

<table>
<thead>
<tr>
<th>Potential Effect on GAHT Drugs</th>
<th>ARV Drugs</th>
<th>GAHT Drugs that may be Affected by ARV Drugs</th>
<th>Clinical Recommendations for GAHT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ARV Drugs with the Least Potential to Impact GAHT Drugs</strong></td>
<td>All NRTIs</td>
<td>None</td>
<td>No dose adjustments necessary. Titrate dose based on desired clinical effects and hormone concentrations.</td>
</tr>
<tr>
<td></td>
<td>Entry Inhibitors:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• IBA</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• MVC</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• T-20</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Unboosted INSTIs:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• BIC</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• DTG</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• RAL</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>NNRTIs:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• RPV</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• DOR</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ARV Drugs that may Increase Concentrations of Some GAHT Drugs</strong></td>
<td>EVG/c All boosted PIs</td>
<td>Dutasteride Finasteride Testosterone</td>
<td>Monitor patient for associated adverse effects; decrease the doses of GAHT drugs as needed to achieve the desired clinical effects and hormone concentrations.</td>
</tr>
<tr>
<td><strong>ARV Drugs that may Decrease Concentrations of GAHT Drugs</strong></td>
<td>PI/r NNRTIs:</td>
<td>Estradiol</td>
<td>Increase the dose of estradiol as needed to achieve the desired clinical effects and hormone concentrations.</td>
</tr>
<tr>
<td></td>
<td>• EFV</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• ETR</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• NVP</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>NNRTIs:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• EFV</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• ETR</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• NVP</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>PI/c</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ARV Drugs with an Unclear Effect on GAHT Drugs</strong></td>
<td>EVG/c PI/c</td>
<td>Estradiol</td>
<td>Increase the doses of GAHT drugs as needed to achieve the desired clinical effects and hormone concentrations.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>There is the potential for increased or decreased estradiol concentrations. Adjust the dose of estradiol to achieve the desired clinical effects and hormone concentrations.</td>
<td></td>
</tr>
</tbody>
</table>

**Note:** See Tables 21a, 21b, 21c, 21d, and 21e for additional information regarding drug-drug interactions between ARV drugs and gender-affirming medications.

**Key:** ARV = antiretroviral; BIC = bictegravir; DOR = doravirine; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; GAHT = gender-affirming hormone therapy; IBA = ibalizumab; INSTI = integrase strand transfer inhibitor; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; RAL = raltegravir; RPV = rilpivirine; T-20 = enfuvirtide
The recommendations in this table for concomitant use of select HIV drugs with FDA-approved HCV DAA drugs are based on available PK interaction data or are predictions based on the known metabolic pathways of the agents. (Instances where PK interaction data are limited or not available are indicated in the table.) Whenever 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 the HCV Guidance for updated information.

**Note:** Interactions with FPV, IDV, NFV, and SQV are **not** included in this table. Please refer to the FDA product labels for information regarding drug interactions with these HIV PIs.

---

### Table 15. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of Hepatitis C Virus in Adults with HIV (page 1 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-Pugh class B or C)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NS5A Inhibitor</td>
<td>NS5B Inhibitor</td>
<td>NS5A/NS5B Inhibitor</td>
</tr>
<tr>
<td>Daclatasvir</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Sofosbuvir</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ledipasvir/Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Sofosbuvir/Velpatasvir</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Sofosbuvir/Velpatasvir/Voxilaprevir</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Glecaprevir/Pibrentasvir</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Elbasvir/Grazoprevir</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Ombitasvir/Paritaprevir/RTV plus Dasabuvir</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>NRTIs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3TC</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>TDF</td>
<td>✓</td>
<td>✓</td>
<td>✓ (Monitor for TDF-associated adverse events.)</td>
</tr>
<tr>
<td>TAF</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>PIs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unboosted ATV</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>
### Table 15. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of Hepatitis C Virus in Adults with HIV (page 2 of 4)

<table>
<thead>
<tr>
<th>Selected HIV Drugs</th>
<th>NS5A Inhibitor</th>
<th>NS5B Inhibitor</th>
<th>HCV Direct-Acting Antiviral Agents</th>
<th>Coformulated</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>NS5A/NS5B Inhibitor</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NS5A/NS5B Inhibitor/NS3/4A PI</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NS5A Inhibitor/ NS3/4A PI</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NS5A Inhibitor/NS3A/4A PI</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NS5A Inhibitor/NS3A/4A PI plus NS5B Inhibitor</td>
<td></td>
</tr>
</tbody>
</table>

#### Pls. continued

<table>
<thead>
<tr>
<th>HIV Drugs</th>
<th>ATV/r or ATV/c</th>
<th>DRV/r or DRV/c</th>
<th>LPV/r</th>
<th>TPV/r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daclatasvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Ledipasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Sofosbuvir/ Velpatasvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Daclatasvir/ Sofosbuvir</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Selected HIV Drugs</td>
<td>NS5A Inhibitor</td>
<td>NS5B Inhibitor</td>
<td>HCV Direct-Acting Antiviral Agents</td>
<td>Coformulated</td>
</tr>
<tr>
<td>-------------------</td>
<td>----------------</td>
<td>----------------</td>
<td>----------------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Daclatasvir</td>
<td>Sofosbuvir</td>
<td>Ledipasvir/ Sofosbuvir</td>
<td>Sofosbuvir/ Velpatasvir</td>
<td>Of osbuvir/ Velpatasvir/ Voxilaprevir</td>
</tr>
</tbody>
</table>

**NNRTIs, continued**

<table>
<thead>
<tr>
<th></th>
<th>Daclatasvir</th>
<th>Sofosbuvir</th>
<th>Ledipasvir</th>
<th>Sofosbuvir</th>
<th>Velpatasvir</th>
<th>Volkaprevir</th>
<th>Gilepervir</th>
<th>Pibrentasvir</th>
<th>Elbasvir</th>
<th>Grazoprevir</th>
<th>Ombitasvir/ Paritaprevir/ RTV plus Dasabuvir</th>
</tr>
</thead>
<tbody>
<tr>
<td>RPV</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>x</td>
</tr>
<tr>
<td>INSTIs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BIC/TAF/FTC</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>DTG</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>EVG/c/TDF/ FTC</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>x</td>
</tr>
<tr>
<td>EVG/c/TAF/ FTC</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>RAL</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>x</td>
</tr>
<tr>
<td>CCR5 Antagonist</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>x</td>
</tr>
</tbody>
</table>

Notes:
- **RPV**
  - **If used with TDF, monitor for TDF-associated adverse events.**

- **INSTIs**
  - **BIC/TAF/FTC**
    - **↓ daclatasvir dose to 30 mg/day**
  - **DTG**
    - **If used with TDF, monitor for TDF-associated adverse events.**
  - **EVG/c/TDF/FTC**
    - **↓ daclatasvir dose to 30 mg/day**
  - **RAL**
  - **CCR5 Antagonist**

- **Should not be used in those with moderate to severe hepatic impairment** (Cirrhosis classified as Child-Pugh class B or C)

- **Gilepervir/ Pibrentasvir**
  - **If used with TDF, monitor for TDF-associated adverse events. Consider monitoring for hepatotoxicity.**
  - **If used with TDF, monitor for TDF-associated adverse events. Consider monitoring for hepatotoxicity.**

- **Elbasvir/ Grazoprevir**
  - **If used with TDF, monitor for TDF-associated adverse events. Consider monitoring for hepatotoxicity.**
  - **Consider monitoring for hepatotoxicity.**

- **Ombitasvir/ Paritaprevir/ RTV plus Dasabuvir**
  - **Consider monitoring for hepatotoxicity.**
  - **Consider monitoring for hepatotoxicity.**
Table 15. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of Hepatitis C Virus in Adults with HIV

<table>
<thead>
<tr>
<th>Drug Combination</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dasabuvir with ombitasvir/paritaprevir/RTV</td>
<td>Dasabuvir must be prescribed with ombitasvir/paritaprevir/RTV.</td>
</tr>
<tr>
<td>Reduce ATV dose to 300 mg and instruct the</td>
<td>Reduce ATV dose to 300 mg and instruct the patient to take it in the morning at the same time as</td>
</tr>
<tr>
<td>patient to take it in the morning at the</td>
<td>ombitasvir/paritaprevir/RTV plus dasabuvir. If RTV cannot be used, choose an alternative HCV</td>
</tr>
<tr>
<td>same time as ombitasvir/paritaprevir/RTV</td>
<td>regimen.</td>
</tr>
<tr>
<td>This HCV regimen contains RTV. If ATV is</td>
<td>This HCV regimen contains RTV. If ATV is part of the ARV regimen, prescribe ATV 300 mg without</td>
</tr>
<tr>
<td>part of the ARV regimen, prescribe ATV 300</td>
<td>COBI or RTV. The modified ARV regimen should be taken in the morning at the same time as Ombitasvir</td>
</tr>
<tr>
<td>mg without COBI or RTV. The modified ARV</td>
<td>/paritaprevir/RTV plus dasabuvir. Resume RTV or COBI regimen when HCV therapy is completed.</td>
</tr>
<tr>
<td>regimen should be taken in the morning at</td>
<td></td>
</tr>
<tr>
<td>the same time as ombitasvir/paritaprevir/RTV</td>
<td></td>
</tr>
<tr>
<td>plus dasabuvir. Resume RTV or COBI regimen</td>
<td></td>
</tr>
<tr>
<td>when HCV therapy is completed.</td>
<td></td>
</tr>
<tr>
<td>Consider using an alternative HCV treatment</td>
<td>Consider using an alternative HCV treatment or ARV regimen to avoid increases in TDF exposure.</td>
</tr>
<tr>
<td>or ARV regimen to avoid increases in TDF</td>
<td>If coadministration is necessary, monitor patient for TDF-associated adverse events.</td>
</tr>
<tr>
<td>exposure.</td>
<td></td>
</tr>
<tr>
<td>Voxilaprevir exposures can increase when it</td>
<td>Voxilaprevir exposures can increase when it is coadministered with pharmacologically boosted DRV</td>
</tr>
<tr>
<td>is coadministered with pharmacologically</td>
<td>or EVG. Until more safety data in clinical settings becomes available, patients who are receiving</td>
</tr>
<tr>
<td>boosted DRV or EVG. Until more safety data</td>
<td>voxilaprevir and pharmacologically boosted DRV or EVG should be monitored for hepatotoxicity.</td>
</tr>
<tr>
<td>in clinical settings becomes available,</td>
<td></td>
</tr>
<tr>
<td>patients who are receiving voxilaprevir and</td>
<td></td>
</tr>
<tr>
<td>EVG should be monitored for hepatotoxicity.</td>
<td></td>
</tr>
<tr>
<td>Consider alternative ARV or HCV regimen.</td>
<td>Consider alternative ARV or HCV regimen. If used together, monitor for HCV efficacy.</td>
</tr>
<tr>
<td>Glecaprevir exposures can increase when it</td>
<td>Glecaprevir exposures can increase when it is coadministered with EVG/c. Until more safety data</td>
</tr>
<tr>
<td>is coadministered with EVG/c. Until more</td>
<td>in clinical settings becomes available, patients who are receiving glecaprevir and EVG/c should</td>
</tr>
<tr>
<td>safety data in clinical settings becomes</td>
<td>be monitored for hepatotoxicity.</td>
</tr>
<tr>
<td>available, patients who are receiving</td>
<td></td>
</tr>
<tr>
<td>glecaprevir and EVG/c should be monitored</td>
<td></td>
</tr>
<tr>
<td>for hepatotoxicity.</td>
<td></td>
</tr>
</tbody>
</table>

Key to Symbols:

- ✓ = ARV agents that can be used concomitantly
- × = ARV agents not recommended
- ? = Data on PK interactions with ARV drug are limited or not available
- ↑ = Increase
- ↓ = Decrease

Key:

- 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; COBI = cobicistat; DAA = direct-acting antiviral agents; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; DSV = dasabuvir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FDA = Food and Drug Administration; FPV = fosamprenavir; FTC = emtricitabine; HCV = hepatitis C virus; IDV = indinavir; INSTI = integrase strand transfer inhibitor; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; PK = pharmacokinetic; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQV = saquinavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV/r = tipranavir/ritonavir
Table 16. 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 care team.</td>
<td>• Care providers, nurses, social workers, case managers, pharmacists, and medication managers.</td>
</tr>
</tbody>
</table>
| Strengthen early linkage to care and retention in care. | • Encourage health care team participation in linkage to and retention in care.  
• Use ARTAS training (if available). |
| Evaluate patient’s knowledge about HIV infection, prevention, and treatment and, based on this assessment, provide HIV-related information. | • 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. |
| Identify facilitators, potential barriers to adherence, and necessary medication management skills both before starting ART and on an ongoing basis. | • Assess patient’s cognitive competence and impairment.  
• 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.  
• Identify and address language and literacy barriers.  
• Assess beliefs, perceptions, and expectations about taking ART (e.g., impact on health, side effects, disclosure issues, consequences of poor adherence).  
• Ask about medication-taking skills and foreseeable challenges with adherence (e.g., past difficulty keeping appointments, adverse effects from previous medications, issues managing other chronic medications, need for medication reminders and organizers).  
• 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. |
| Provide needed resources. | • Provide or refer for mental health and/or substance abuse treatment.  
• Provide resources about stable housing, social support, transportation assistance, and income and food security. |
| Involve the patient in ARV regimen selection. | • Review potential side effects, dosing frequency, pill burden, storage requirements, food requirements, and consequences of poor adherence.  
• Assess daily activities and tailor regimen to predictable and routine daily events.  
• Consider preferential use of PI/r-based or DTG-based ART if poor adherence is anticipated.  
• Consider use of STR formulations.  
• Assess if cost/copayment for drugs will affect adherence and access to medications. |
| Assess adherence at every clinic visit. | • Monitor viral load as a strong biologic measure of adherence.  
• Use a simple behavioral rating scale or self-reported assessment.  
• Employ a structured format that normalizes or assumes less-than-perfect adherence and minimizes socially desirable or “white-coat adherence” responses.  
• Ensure that other members of the health care team also assess and support adherence. |
| Use positive reinforcement to foster adherence success. | • Inform patients of low or nondetectable levels of HIV viral load and increases in CD4 cell counts.  
• Thank patients for attending their appointments. |
Table 16. 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>
<tbody>
<tr>
<td>Identify the type of and reasons for poor adherence and target ways to</td>
<td>• Failure to understand dosing instructions.</td>
</tr>
<tr>
<td>improve adherence.</td>
<td>• Complexity of regimen (e.g., pill burden, size, dosing schedule, food requirements, polypharmacy).</td>
</tr>
<tr>
<td></td>
<td>• Pill aversion or pill fatigue.</td>
</tr>
<tr>
<td></td>
<td>• Adverse effects.</td>
</tr>
<tr>
<td></td>
<td>• Inadequate understanding of drug resistance and its relationship to adherence.</td>
</tr>
<tr>
<td></td>
<td>• Patient is unaware of appointments or appointments are not scheduled with proper patient input.</td>
</tr>
<tr>
<td></td>
<td>• Cost-related issues (copays for medications or visits, missed work time).</td>
</tr>
<tr>
<td></td>
<td>• Depression, drug and alcohol use, homelessness, poverty.</td>
</tr>
<tr>
<td></td>
<td>• Stigma of taking pills or attending HIV-related appointments.</td>
</tr>
<tr>
<td></td>
<td>• Nondisclosure of status leading to missed doses, refills, or appointments.</td>
</tr>
<tr>
<td>Select from among available effective adherence and retention interventions.</td>
<td>• See <a href="https://www.cdc.gov/hiv/research/interventionresearch/compendium/index.html">https://www.cdc.gov/hiv/research/interventionresearch/compendium/index.html</a> for a summary of best practice interventions to improve linkage, retention, and adherence.</td>
</tr>
<tr>
<td></td>
<td>• Use adherence-related tools to complement education and counseling interventions (e.g., text messaging, pill box monitors, pill boxes, alarms).</td>
</tr>
<tr>
<td></td>
<td>• Use community resources to support adherence (e.g., visiting nurses, community workers, family, peer advocates, transportation assistance).</td>
</tr>
<tr>
<td></td>
<td>• Use patient prescription assistance programs (see above, under “Provide needed resources”).</td>
</tr>
<tr>
<td></td>
<td>• Use motivational interviews.</td>
</tr>
<tr>
<td></td>
<td>• Provide outreach for patients who drop out of care</td>
</tr>
<tr>
<td></td>
<td>• Use peer or paraprofessional treatment navigators.</td>
</tr>
<tr>
<td></td>
<td>• Recognize positive clinical outcomes resulting from better adherence.</td>
</tr>
<tr>
<td></td>
<td>• Arrange for DOT in persons in substance use treatment (if feasible).</td>
</tr>
<tr>
<td></td>
<td>• Enhance clinic support and structures to promote linkage and retention (reminder calls, flexible scheduling, open access, active referrals, and improved patient satisfaction).</td>
</tr>
<tr>
<td>Systematically monitor retention in care.</td>
<td>• Record and follow up on missed visits.</td>
</tr>
</tbody>
</table>

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 17. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy (page 1 of 5)

Adverse effects for ARV drugs that are no longer commonly used in clinical practice (ddI, d4T, FPV/r, IDV, NFV, SQV/r, and TPV/r) have been removed from this table, with the exception of lipodystrophy and peripheral neuropathy associated with ddI and d4T. Because these effects may persist long after discontinuation of ddI or d4T, and patients may still present with these long-lasting toxicities, the drugs remain listed among the ARVs associated with these two effects. Refer to the product labels or to the July 10, 2019, version of the guidelines (found in the archived guidelines section of AIDSinfo) for information regarding the adverse effects associated with these older ARVs.

This table focuses on ARV-associated adverse effects that a patient may experience as a result of taking an ARV regimen. For information regarding potential adverse effects of ARVs on fetuses and newborns when certain ARVs are taken around the time of conception or during pregnancy, refer to Table 6b and to the Perinatal Guidelines.

In this table, N/A indicates either that there are no reported cases for that particular side effect or that data for that specific ARV drug class are not available. See Appendix B, Tables 3-9 for additional information listed by drug.

<table>
<thead>
<tr>
<th>Adverse Effect</th>
<th>Drug Class</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NRTIs</td>
</tr>
<tr>
<td>Bone Density Effects</td>
<td>TDF:</td>
</tr>
<tr>
<td></td>
<td>TAF:</td>
</tr>
<tr>
<td></td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>ZDV:</td>
</tr>
<tr>
<td></td>
<td>RPV,</td>
</tr>
<tr>
<td></td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ABC:</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 7/3/2020
Table 17. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy (page 2 of 5)

<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>Cholelithiasis</td>
<td>N/A</td>
<td>N/A</td>
<td>ATV: Cholelithiasis and kidney stones may present concurrently. Median onset is 42 months after ARV initiation.</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Diabetes Mellitus and Insulin Resistance</td>
<td>ZDV</td>
<td>N/A</td>
<td>LPV/r, but not with boosted ATV or DRV</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>ZDV &gt; ABC: ↑ TG and ↑ LDL and ↑ HDL (no change in TC:HDL ratio)</td>
<td>TAF: ↑ TG, ↑ LDL, and ↑ HDL (no change in TC:HDL ratio)</td>
<td>EFV: ↑ TG, ↑ LDL, ↑ HDL</td>
<td>EVG/c: ↑ TG, ↑ LDL, ↑ HDL</td>
<td>N/A</td>
</tr>
<tr>
<td>Gastrointestinal Effects</td>
<td>ZDV &gt; Other NRTIs: Nausea and vomiting</td>
<td>N/A</td>
<td>GI intolerance (e.g., diarrhea, nausea, vomiting)</td>
<td>IBA: In a study of 40 people, 8% of patients reported diarrhea.</td>
<td></td>
</tr>
<tr>
<td>Hepatic Effects</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. ZDV: Steatosis</td>
<td>EFV: Most cases relate to an increase in transaminases. Fulminant hepatitis leading to death or hepatic failure requiring transplantation have been reported. NVP: Severe hepatotoxicity associated with skin rash or hypersensitivity. A 2-week NVP dose escalation may reduce risk. Risk is greater for women with pre-NVP CD4 counts &gt;250 cells/mm³ and men with pre-NVP CD4 counts &gt;400 cells/mm³. NVP should never be used for post-exposure prophylaxis. EFV and NVP are not recommended in patients with hepatic insufficiency (Child-Pugh class B or C).</td>
<td>All Pls: Drug-induced hepatitis and hepatic decompensation have been reported. ATV: Jaundice due to indirect hyperbilirubinemia</td>
<td>DTG: Persons with HBV or HCV coinfection may be at higher risk of DTG-associated hepatotoxicity.</td>
<td>MVC: Hepatotoxicity with or without rash or HSRs reported.</td>
</tr>
</tbody>
</table>
### Table 17. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy (page 3 of 5)

<table>
<thead>
<tr>
<th>Adverse Effect</th>
<th>Drug Class</th>
<th>NRTIs</th>
<th>NNRTIs</th>
<th>PI</th>
<th>INSTIs</th>
<th>Els</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hypersensitivity Reaction</strong>&lt;br&gt;Excluding rash alone or Stevens-Johnson syndrome</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABC: Contraindicated if patient is HLA-B*5701 positive. Median onset for HSR is 9 days after treatment initiation; 90% of reactions occur within 6 weeks.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HSR Symptoms (in Order of Descending Frequency): Fever, rash, malaise, headache, myalgia, chills, diarrhea, vomiting, abdominal pain, dyspnea, arthralgia, and respiratory symptoms</td>
<td>NVP: Hypersensitivity syndrome of hepatotoxicity and rash that may be accompanied by fever, general malaise, fatigue, myalgias, arthralgias, blisters, oral lesions, conjunctivitis, facial edema, eosinophilia, renal dysfunction, granulocytopenia, or lymphadenopathy. Risk is greater for ARV-naive women with pre-NVP CD4 counts &gt;250 cells/mm³ and men with pre-NVP CD4 counts &gt;400 cells/mm³. Overall, risk is higher for women than men. A 2-week dose escalation of NVP reduces risk.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptoms worsen with continuation of ABC.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients should not be rechallenged with ABC if HSR is suspected, regardless of their HLA-B*5701 status.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Lactic Acidosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reported with Older NRTIs, d4T, ZDV, and ddI, but not with ABC, 3TC, FTC, TAF, or TDF.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lipoatrophy: Associated with history of exposure to d4T or ZDV (d4T &gt; ZDV). Not reported with ABC, 3TC or FTC, TAF or TDF.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lipohypertrophy: Trunk fat increase observed with EFV-, PI-, and RAL-containing regimens; however, causal relationship has not been established.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Myopathy/ Elevated Creatine Phosphokinase</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ZDV: Myopathy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAL and DTG: ↑ CPK, rhabdomyolysis, and myopathy or myositis have been reported.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MVC: HSR reported as part of a syndrome related to hepatotoxicity.</td>
<td></td>
<td></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 7/3/2020
### Table 17. 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>Pls</th>
<th>INSTIs</th>
<th>Els</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nervous System/ Psychiatric Effects</strong></td>
<td>History of Exposure to ddI, ddC, or d4T: Peripheral neuropathy (can be irreversible)</td>
<td>Neuropsychiatric Events: EFV &gt; RPV, DOR, ETR</td>
<td>EFV: Somnolence, insomnia, abnormal dreams, dizziness, impaired concentration, depression, psychosis, suicidal ideation, ataxia, encephalopathy. Some symptoms may subside or diminish after 2–4 weeks. Bedtime dosing and taking without food may reduce symptoms. Risk factors include psychiatric illness, concomitant use of agents with neuropsychiatric effects, and genetic factors.</td>
<td>RPV: Depression, suicidality, sleep disturbances</td>
<td>DOR: Sleep disorders and disturbances, dizziness, altered sensorium; depression and suicidality and self-harm</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>N/A</td>
<td>All INSTIs: Insomnia, depression, and suicidality have been reported with INSTI use, primarily in patients with pre-existing psychiatric conditions.</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Rash</strong></td>
<td>FTC: Hyperpigmentation</td>
<td>All NNRTIs</td>
<td>ATV, DRV, and LPV/r</td>
<td>All INSTIs</td>
<td>MVC, IBA</td>
</tr>
<tr>
<td></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.</td>
<td>RPV: Inhibits Cr secretion without reducing renal glomerular function.</td>
<td>ATV and LPV/r: Associated with increased risk of chronic kidney disease in a large cohort study.</td>
<td>DTG, COBI (as a Boosting Agent for EVG), and BIC: Inhibits Cr secretion without reducing renal glomerular function.</td>
<td>IBA: SCR abnormalities ≥ Grade 3 reported in 10% of trial participants.</td>
</tr>
<tr>
<td><strong>Renal Effects/ Urolithiasis</strong></td>
<td>TAF: Less impact on renal biomarkers and lower rates of proteinuria than TDF.</td>
<td></td>
<td>ATV: Stone or crystal formation. Adequate hydration may reduce risk.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Table 17. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy (page 5 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>Stevens-Johnson Syndrome/Toxic Epidermal Necrosis</td>
<td>N/A</td>
<td>NVP &gt; EFV, ETR, RPV</td>
<td>Some reported cases for DRV, LPV/r, and ATV</td>
<td>RAL</td>
<td>N/A</td>
</tr>
<tr>
<td>Weight Gain</td>
<td>Weight gain has been associated with initiation of ART and subsequent viral suppression. The increase appears to be greater with INSTIs than with other drug classes. Greater weight increase has also been reported with TAF than with TDF, and greater with DOR than EFV.</td>
<td>INSTI &gt; other ARV drug classes</td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 18. Antiretroviral Therapy-Associated Adverse Effects That Can Be Managed with Substitution of Alternative Antiretroviral Agents

This table focuses on ARV-associated adverse effects that patients may experience as a result of a current ARV regimen. For information regarding ARV choices to use in individuals of childbearing potential and during pregnancy to avoid potential ARV adverse effects on fetuses and newborns refer to Table 6b and to the Perinatal Guidelines.

<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>Bone Density Effects</strong></td>
<td></td>
<td>TDF&lt;sup&gt;a&lt;/sup&gt;</td>
<td>TAF or ABC&lt;sup&gt;b&lt;/sup&gt;</td>
<td>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>Regimen not including ZDV</td>
<td>ZDV has been associated with neutropenia and macrocytic anemia.</td>
<td></td>
</tr>
<tr>
<td><strong>Calculi</strong></td>
<td>ATV, ATV/c, ATV/r</td>
<td>DRV/c, DRV/r, INSTI, or NNRTI</td>
<td>This switch should be made if ATV is the presumed cause of the calculi.</td>
<td></td>
</tr>
<tr>
<td><strong>Cardiac QTc Interval Prolongation</strong></td>
<td>EFV, RPV</td>
<td>Boosted ATV or DRV, DOR, or INSTI-based regimen</td>
<td>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>
<td></td>
</tr>
<tr>
<td><strong>Cardiovascular Events</strong></td>
<td>ABC</td>
<td>TDF or TAF</td>
<td>ABC use has been associated with CV disease and cardiac events in some, but not all, observational studies. TDF has been associated with lower lipid levels than TAF. If lipids are a concern, see Dyslipidemia below. 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>
<td></td>
</tr>
<tr>
<td><strong>Dyslipidemia</strong></td>
<td>RTV- or COBI-boosted PI regimens, EFV</td>
<td>BIC, DTG, RAL, DOR, or RPV</td>
<td>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>
<td></td>
</tr>
<tr>
<td><strong>Gastrointestinal Effects</strong></td>
<td>LPV/r</td>
<td>Boosted ATV or DRV, INSTI, NNRTI</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 ARV substitution unless they are persistent and intolerable. 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>
<td></td>
</tr>
</tbody>
</table>

Downloaded from [https://aidsinfo.nih.gov/guidelines](https://aidsinfo.nih.gov/guidelines) on 7/3/2020
Table 18. Antiretroviral Therapy-Associated Adverse Effects That Can Be Managed with Substitution of Alternative Antiretroviral Agents  

<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>Hypersensitivity Reaction</strong></td>
<td>ABC, EFV, ETR, NVP, RPV</td>
<td>Any appropriate ABC-sparing regimen</td>
<td>Non-NNRTI ART</td>
<td>Never rechallenge with ABC following a suspected HSR, regardless of the patient’s HLA-B*5701 status. Risk of HSR with NVP is higher for women and those with high CD4 counts. Reactions to NVP, ETR, RAL, DTG, and MVC may be accompanied by elevated liver transaminases.</td>
</tr>
<tr>
<td></td>
<td>DTG, RAL, MVC</td>
<td>Non-INSTI ART</td>
<td>Suitable alternative ART</td>
<td></td>
</tr>
<tr>
<td><strong>Insulin Resistance</strong></td>
<td>LPV/r</td>
<td>INSTI, NNRTI</td>
<td></td>
<td>Results of switch studies have been inconsistent. Studies in HIV-negative patients suggest a direct causal effect of LPV/r on insulin resistance. However, traditional risk factors for insulin resistance may be stronger risk factors than the use of any PI.</td>
</tr>
<tr>
<td><strong>Jaundice and Icterus</strong></td>
<td>ATV, ATV/c, ATV/r</td>
<td>DRV/c, DRV/r, INSTI, or NNRTI</td>
<td></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>Peripheral lipoatrophy (loss of subcutaneous fat of the limbs, face, and buttocks) is associated with prior thymidine analog (d4T and ZDV) use. Despite switching from these ARVs, fat recovery remains slow (may take years) and incomplete.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Lipohypertrophy</strong></td>
<td>Accumulation of visceral, truncal, dorsocervical, 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 lipohypertrophy.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Neuropsychiatric Side Effects</strong></td>
<td>EFV, RPV</td>
<td>DOR, ETR, PI/c, or PI/r</td>
<td></td>
<td>In most patients, EFV-related CNS effects subside within 4 weeks after initiation of the drug, but in some patients, ataxia or encephalopathy may appear months to years after EFV-initiation. Persistent or intolerable effects should prompt substitution of EFV. INSTIs are associated with insomnia. Depression and suicidality have been infrequently reported with INSTI use, primarily in patients with pre-existing psychiatric conditions.</td>
</tr>
<tr>
<td>Dizziness, suicidal ideation, abnormal dreams, depression, ataxia, encephalopathy</td>
<td>DRV/c, DRV/r</td>
<td>INSTI-based regimen</td>
<td></td>
<td>Mild rashes that develop 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></td>
<td>ATC/c, ATP/r, or another drug class (e.g., INSTI)</td>
<td></td>
<td></td>
<td>Mild rashes following DRV/r use may resolve without modification of therapy. For more severe reactions, change to an alternative boosted PI or an agent from another drug class.</td>
</tr>
<tr>
<td><strong>Rash</strong></td>
<td>NNRTIs (especially NVP and EFV)</td>
<td>ABC, TAF (for patients with CrCl &gt;50 mL/min, unless on chronic hemodialysis), NRTI-sparing regimens, or regimens using only 3TC or FTC as the NRTI may be considered if appropriate.</td>
<td></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. COBI, DTG, BIC, and, to a lesser extent, RPV, can increase SCr through inhibition of creatinine secretion. This effect does not affect glomerular filtration. However, assess patient for renal dysfunction if SCr increases by &gt;0.4 mg/dL.</td>
</tr>
<tr>
<td></td>
<td>DRV/c, ATP/r, LPV/r</td>
<td>BIC, DTG, EVG/cTAF/FTC, RAL, boosted DRV, or NNRTI</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](https://aidsinfo.nih.gov/guidelines) on 7/3/2020
Table 18. Antiretroviral Therapy-Associated Adverse Events That Can Be Managed with Substitution of Alternative Antiretroviral Agents  (page 3 of 3)

<table>
<thead>
<tr>
<th>Event</th>
<th>Alternative Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>In patients with chronic active HBV infection, another agent that is active against HBV should be substituted for TDF.</td>
<td>another agent that is active against HBV</td>
</tr>
<tr>
<td>ABC should be used only in patients known to be HLA-B*5701 negative.</td>
<td>ABC should be used only in patients known to be HLA-B*5701 negative.</td>
</tr>
<tr>
<td>TDF reduces ATV levels; therefore, unboosted ATV should not be coadministered with TDF.</td>
<td>TDF reduces ATV levels; therefore, unboosted ATV should not be coadministered with TDF.</td>
</tr>
</tbody>
</table>

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; BMD = bone mineral density; CD4 = CD4 T lymphocyte; CNS = central nervous system; COBI = cobicistat; CrCl = creatine clearance; CV = cardiovascular; d4T = stavudine; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FPV = fosamprenavir; 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; NRTI = 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; TC = total cholesterol; TDF = tenofovir disoproxil fumarate; TG = triglycerides; ZDV = zidovudine
Table 19a. Insurance and Health Program Prescription Drug Pricing and Access  (page 1 of 2)

<table>
<thead>
<tr>
<th>Insurance/Health Program</th>
<th>Prescription Drug Pricing and Access</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medicaid</td>
<td>Drug manufacturers must participate in MDRP for their drugs to be covered by Medicaid and under Medicare Part B. Manufacturers are required to pay Medicaid programs a rebate of at least 23.1% of the average price paid to manufacturers by wholesalers (AMP) for most brand-name drugs sold to retail pharmacies (13% for generics). Manufacturers pay additional rebates if this confidential AMP increases faster than the CPI-U rate of inflation. States are permitted to require “nominal” cost-sharing for medical and pharmacy benefits for some beneficiaries though many elect not to do so. States can obtain a waiver to allow them to apply higher cost-sharing.</td>
</tr>
<tr>
<td>Medicare</td>
<td>ARVs are one of six “protected drug classes” under Medicare Part D. Part D plans must provide access to all, or substantially all, FDA-approved ARVs. Part D plan sponsors, or PBMs on their behalf, negotiate rebates on outpatient drugs with manufacturers; the extent of rebating is unclear. Most physician-administered drugs and biologics are covered under Medicare Part B at a set cost: ASP plus 6%. This pricing mechanism controls spending by narrowing the spread between what is actually paid for the drug and what is actually billed to Medicare. Premiums and cost-sharing payments may be significant for both services and prescription drugs; there is no cap on out-of-pocket spending under Part A (hospital care) and Part B. Some subsidies and supplemental coverage are offered for low-income beneficiaries. Manufacturer copay assistance programs cannot be applied to Part B or Part D cost sharing; cost sharing support is available from ADAPs, foundations, and other sources, based on financial eligibility criteria.</td>
</tr>
<tr>
<td>Commercial Insurance</td>
<td>Private insurance plans, or PBMs on their behalf, negotiate rebates on inpatient and outpatient drugs with manufacturers; the extent of rebating is unclear. Formulary restrictions and utilization management (prior authorization, step therapy, higher cost sharing) are possible as cost-containment measures. Cost sharing can be highly variable. Manufacturer copay assistance programs can be applied in most cases but may not count toward annual Affordable Care Act cost sharing limits; cost sharing support is also available from ADAPs, foundations, and other sources based on financial eligibility criteria.</td>
</tr>
</tbody>
</table>
### Table 19a. Insurance and Health Program Prescription Drug Pricing and Access

<table>
<thead>
<tr>
<th>Insurance/Health Program</th>
<th>Prescription Drug Pricing and Access</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ADAPs</strong></td>
<td>Significant discounting on most ARVs negotiated by the ADAP Crisis Task Force is allowed under the 340B Drug Pricing Program.</td>
</tr>
<tr>
<td></td>
<td>There is usually no cost sharing for ADAP clients who are uninsured. ADAP can assist with commercial or public insurance out-of-pocket costs.</td>
</tr>
<tr>
<td><strong>Veterans Affairs</strong></td>
<td>The FCP is the maximum price manufacturers may charge the four largest federal purchasers of pharmaceuticals (the “Big Four”): The Department of Veterans Affairs, the Department of Defense, the Public Health Service (including the Indian Health Service), and the Coast Guard. The FCP of a drug includes a 24% discount on a drug’s average price paid by non-federal purchasers. Additional discounts may be applied if non-federal purchase prices increase faster than the CPI-U inflation rate.</td>
</tr>
<tr>
<td></td>
<td>Big Four prices may be 40% to 50% below list prices. VA may negotiate further price reductions.</td>
</tr>
<tr>
<td></td>
<td>Prescription drug cost sharing is generally nominal; medications are not withheld from those who cannot afford cost sharing expenses.</td>
</tr>
<tr>
<td><strong>Community Health Centers</strong></td>
<td>Many community health centers are enrolled in the 340B Drug Pricing Program, which allows for discounted drug purchasing using the MDRP formula.</td>
</tr>
<tr>
<td></td>
<td>Discounts start at 23.1% off AMP, with additional discounts if the AMP increases faster than the CPI-U rate of inflation.</td>
</tr>
<tr>
<td></td>
<td>Cost-sharing in community health centers is first driven by payer source. For clients who are uninsured, cost-sharing, if required, is typically based on a sliding fee scale.</td>
</tr>
</tbody>
</table>

**Key:** ADAP = AIDS Drug Assistance Programs; AMP = average manufacturer price; ARV = antiretroviral; ASP = average sales price; CPI-U = consumer price index-urban; FCP = Federal Ceiling Price; FDA = Food and Drug Administration; MDRP = Medicaid Drug Rebate Program; PBM = pharmacy benefits manager; VA = Veterans Affairs
Table 19b. Monthly Average Prices of Commonly Used Antiretroviral Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 1 of 5)

Table 19b includes three benchmark prices, rounded to the nearest dollar, for commonly used ARV drugs as a general reference for health care providers when considering the cost of HIV treatment. Health care providers should contact patients’ pharmacies or payers regarding actual prices, comparative cost savings, formulary restrictions, and patient cost-sharing requirements.

Wholesale acquisition cost (WAC) is the list price published by manufacturers for prescription drugs or biologics sold to wholesalers. The WAC price approximates what retail pharmacies pay wholesalers for single-source (e.g., brand-name) drugs. There is a range of WAC prices for generic ARV drugs, as these are multiple-source products with variable list prices. With increasing competition, actual transactional prices of generic drugs among wholesalers and pharmacies decrease substantially. Average wholesale price (AWP) has historically been used as the basis for setting public (e.g., Medicaid) and private (e.g., commercial insurer) reimbursement rates for pharmacies. Neither WAC nor AWP include variable price concessions along supply and payment chains, including discounts and rebates to wholesalers, pharmacies, federal purchasers (e.g., the Veterans’ Administration), pharmacy benefit managers (PBMs), commercial insurers, Medicaid, 340B pharmacies, and AIDS Drug Assistance Programs. The availability of these discounts and rebates depends on product demand, market competition, and WAC price increases set by manufacturers. Maximum prices are assigned to generic products with three or more therapeutically and pharmaceutically equivalent products, as determined by the Food and Drug Administration. This federally established price is the federal upper limit (FUL). Federal Medicaid will reimburse state Medicaid programs up to this limit for multiple-source drugs (plus the dispensing fee); commercial insurers set their own reimbursement upper limits with pharmacies. Whereas WACs and AWPs are generally set annually, FULs are adjusted on a monthly basis, particularly for multiple-source drugs with fluctuating pharmacy acquisition costs. In the table below, the FUL for a drug is described as “pending” if a generic drug currently lacks the competition required to trigger a FUL.

<table>
<thead>
<tr>
<th>ARV Drug (Generic and Brand Names)</th>
<th>Strength, Formulation</th>
<th>Tablets, Capsules, or mLs per Month</th>
<th>WAC (Monthly)b</th>
<th>AWP (Monthly)b</th>
<th>FUL (As of Oct. 31, 2019)c</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NRTIs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abacavir</td>
<td>300 mg tablet</td>
<td>60 tablets</td>
<td>$150 to $482</td>
<td>$502 to $603</td>
<td>$43</td>
</tr>
<tr>
<td>• Generic</td>
<td>60 tablets</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Ziagen</td>
<td>300 mg tablet</td>
<td>60 tablets</td>
<td>$559</td>
<td>$670</td>
<td></td>
</tr>
<tr>
<td>Emtricitabine</td>
<td>200 mg capsule</td>
<td>30 capsules</td>
<td>$537</td>
<td>$644</td>
<td>N/A</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>300 mg tablet</td>
<td>30 tablets</td>
<td>$75 to $343</td>
<td>$324 to $430</td>
<td>$51</td>
</tr>
<tr>
<td>• Generic</td>
<td>30 tablets</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Epivir</td>
<td>300 mg tablet</td>
<td>30 tablets</td>
<td>$416</td>
<td>$499</td>
<td></td>
</tr>
<tr>
<td>Tenofovir Disoproxil Fumarate</td>
<td>300 mg tablet</td>
<td>30 tablets</td>
<td>$27 to $163</td>
<td>$110 to $1,216</td>
<td>$203</td>
</tr>
<tr>
<td>• Generic</td>
<td>30 tablets</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Viread</td>
<td>300 mg tablet</td>
<td>30 tablets</td>
<td>$1,196</td>
<td>$1,435</td>
<td></td>
</tr>
<tr>
<td>• Generic</td>
<td>30 tablets</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 7/3/2020
Table 19b. Monthly Average Prices of Commonly Used Antiretroviral Drugs *(Last updated December 18, 2019; last reviewed December 18, 2019)* (page 2 of 5)

<table>
<thead>
<tr>
<th>ARV Drug (Generic and Brand Names)</th>
<th>Strength, Formulation</th>
<th>Tablets, Capsules, or mLs per Month</th>
<th>WAC (Monthly)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>AWP (Monthly)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>FUL (As of Oct. 31, 2019)&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NRTIs, continued</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zidovudine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Generic</td>
<td>300 mg tablet</td>
<td>60 tablets</td>
<td>$36 to $54</td>
<td>$54 to $365</td>
<td>$13</td>
</tr>
<tr>
<td><strong>NRTI Combination Products</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abacavir/Lamivudine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Generic</td>
<td>600 mg/300 mg tablet</td>
<td>30 tablets</td>
<td>$185 to $1,116</td>
<td>$1,393 to $1,550</td>
<td>$182</td>
</tr>
<tr>
<td>• Epzicom</td>
<td>600 mg/300 mg tablet</td>
<td>30 tablets</td>
<td>$1,292</td>
<td>$1,550</td>
<td></td>
</tr>
<tr>
<td><strong>Tenofovir Alafenamide/Emtricitabine</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Truvada</td>
<td>300 mg/200 mg tablet</td>
<td>30 tablets</td>
<td>$1,676</td>
<td>$2,011</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Tenofovir Disoproxil Fumarate/Emtricitabine</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Cimduo</td>
<td>300 mg/300 mg tablet</td>
<td>30 tablets</td>
<td>$1,005</td>
<td>$1,207</td>
<td>N/A</td>
</tr>
<tr>
<td>• Temixys</td>
<td>300 mg/300 mg tablet</td>
<td>30 tablets</td>
<td>$850</td>
<td>$1,020</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Zidovudine/Lamivudine</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Generic</td>
<td>300 mg/150 mg tablet</td>
<td>60 tablets</td>
<td>$134 to $578</td>
<td>$878 to $932</td>
<td>$123</td>
</tr>
<tr>
<td>• Combivir</td>
<td>300 mg/150 mg tablet</td>
<td>60 tablets</td>
<td>$901</td>
<td>$1,082</td>
<td></td>
</tr>
<tr>
<td><strong>NNRTIs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Efavirenz</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Generic</td>
<td>600 mg tablet</td>
<td>30 tablets</td>
<td>$894 to $980</td>
<td>$1,073 to $1,117</td>
<td>$768</td>
</tr>
<tr>
<td>• Sustiva</td>
<td>600 mg tablet</td>
<td>30 tablets</td>
<td>$981</td>
<td>$1,177</td>
<td></td>
</tr>
<tr>
<td>Doravirine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Pifeltro</td>
<td>100 mg tablet</td>
<td>30 tablets</td>
<td>$1,380</td>
<td>$1,656</td>
<td>N/A</td>
</tr>
<tr>
<td>Etravirine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Intelence</td>
<td>200 mg tablet</td>
<td>60 tablets</td>
<td>$1,366</td>
<td>$1,628</td>
<td>N/A</td>
</tr>
</tbody>
</table>
Table 19b. Monthly Average Prices of Commonly Used Antiretroviral Drugs (Last updated December 18, 2019; last reviewed December 18, 2019)  

<table>
<thead>
<tr>
<th>ARV Drug (Generic and Brand Names)</th>
<th>Strength, Formulation</th>
<th>Tablets, Capsules, or mLs per Month</th>
<th>WAC (Monthly)(^b)</th>
<th>AWP (Monthly)(^b)</th>
<th>FUL (As of Oct. 31, 2019)(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NNRTIs, continued</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nevirapine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Generic</td>
<td>200 mg tablet</td>
<td>60 tablets</td>
<td>$10 to $45</td>
<td>$648 to $651</td>
<td>$65</td>
</tr>
<tr>
<td>- Viramune</td>
<td>200 mg tablet</td>
<td>60 tablets</td>
<td>$906</td>
<td>$1,087</td>
<td></td>
</tr>
<tr>
<td>- Generic XR</td>
<td>400 mg tablet</td>
<td>30 tablets</td>
<td>$135 to $565</td>
<td>$595 to $706</td>
<td></td>
</tr>
<tr>
<td>- Viramune XR</td>
<td>400 mg tablet</td>
<td>30 tablets</td>
<td>$840</td>
<td>$1,008</td>
<td>$392</td>
</tr>
<tr>
<td><strong>Rilpivirine</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Edurant</td>
<td>25 mg tablet</td>
<td>30 tablets</td>
<td>$1,115</td>
<td>$1,338</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>PIs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atazanavir</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Generic</td>
<td>200 mg capsule</td>
<td>60 capsules</td>
<td>$445 to $1,264</td>
<td>$1,517 to $1,668</td>
<td>$1,405</td>
</tr>
<tr>
<td>- Reyataz</td>
<td>200 mg capsule</td>
<td>60 capsules</td>
<td>$1,463</td>
<td>$1,756</td>
<td></td>
</tr>
<tr>
<td>- Generic</td>
<td>300 mg capsule</td>
<td>30 capsules</td>
<td>$445 to $1,252</td>
<td>$1,502 to $1,652</td>
<td></td>
</tr>
<tr>
<td>- Reyataz</td>
<td>300 mg capsule</td>
<td>30 capsules</td>
<td>$1,449</td>
<td>$1,739</td>
<td></td>
</tr>
<tr>
<td><strong>Atazanavir/Cobicistat</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Evotaz</td>
<td>300/150 mg tablet</td>
<td>30 tablets</td>
<td>$1,605</td>
<td>$1,927</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Darunavir</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Prezista</td>
<td>600 mg tablet</td>
<td>60 capsules</td>
<td>$1,690</td>
<td>$2,028</td>
<td>N/A</td>
</tr>
<tr>
<td>- Prezista</td>
<td>800 mg tablet</td>
<td>30 tablets</td>
<td>$1,690</td>
<td>$2,028</td>
<td>N/A</td>
</tr>
<tr>
<td>- Prezista</td>
<td>100 mg/mL suspension</td>
<td>200 mL</td>
<td>$939</td>
<td>$1,126</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Darunavir/Cobicistat</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Prezobix</td>
<td>800 mg/150 mg tablet</td>
<td>30 tablets</td>
<td>$1,931</td>
<td>$2,317</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Lopinavir/Ritonavir</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Kaletra</td>
<td>200 mg/50 mg tablet</td>
<td>120 tablets</td>
<td>$1,024</td>
<td>$1,229</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Tipranavir</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Aptivus</td>
<td>250 mg capsule</td>
<td>120 capsules</td>
<td>$1,673</td>
<td>$2,008</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>INSTIs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dolutegravir</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Tivicay</td>
<td>50 mg tablet</td>
<td>30 tablets</td>
<td>$1,740</td>
<td>$2,089</td>
<td>N/A</td>
</tr>
<tr>
<td>ARV Drug (Generic and Brand Names)</td>
<td>Strength, Formulation</td>
<td>Tablets, Capsules, or mLs per Month</td>
<td>WAC (Monthly)(^b)</td>
<td>AWP (Monthly)(^b)</td>
<td>FUL (As of Oct. 31, 2019)(^c)</td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>-----------------------</td>
<td>-----------------------------------</td>
<td>-------------------</td>
<td>-------------------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td><strong>INSTIs, continued</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tivicay</td>
<td>50 mg tablet</td>
<td>60 tablets</td>
<td>$3,480</td>
<td>$4,178</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Raltegravir</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isentress</td>
<td>400 mg tablet</td>
<td>60 tablets</td>
<td>$1,574</td>
<td>$1,889</td>
<td>N/A</td>
</tr>
<tr>
<td>Isentress HD</td>
<td>600 mg tablet</td>
<td>60 tablets</td>
<td>$1,574</td>
<td>$1,889</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Fusion Inhibitor</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enfuvirtide</td>
<td>90 mg injection kit</td>
<td>60 doses (1 kit)</td>
<td>$3,586</td>
<td>$4,303</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>CCR5 Antagonist</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maraviroc</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Selzentry</td>
<td>150 mg tablet</td>
<td>60 tablets</td>
<td>$1,556</td>
<td>$1,867</td>
<td>N/A</td>
</tr>
<tr>
<td>Selzentry</td>
<td>300 mg tablet</td>
<td>60 tablets</td>
<td>$1,556</td>
<td>$1,867</td>
<td>N/A</td>
</tr>
<tr>
<td>Selzentry</td>
<td>300 mg tablet</td>
<td>120 tablets</td>
<td>$3,112</td>
<td>$3,734</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>CD4-Directed Post-Attachment Inhibitor</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ibalizumab-uiyk</td>
<td>200 mg vial</td>
<td>8 vials</td>
<td>$9,080</td>
<td>$10,896</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Coformulated Combination Products as Single-Tablet Regimens</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bictegravir/Tenofovir Alafenamide/Emtricitabine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biktarvy</td>
<td>50 mg/25 mg/200 mg tablet</td>
<td>30 tablets</td>
<td>$3,089</td>
<td>$3,707</td>
<td>N/A</td>
</tr>
<tr>
<td>Darunavir/Cobicistat/Tenofovir Alafenamide/Emtricitabine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symtuza</td>
<td>800 mg/150 mg/10 mg/200 mg tablet</td>
<td>30 tablets</td>
<td>$3,722</td>
<td>$4,466</td>
<td>N/A</td>
</tr>
<tr>
<td>Dolutegravir/Abacavir/Lamivudine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triumeq</td>
<td>50 mg/600 mg/300 mg tablet</td>
<td>30 tablets</td>
<td>$2,889</td>
<td>$3,467</td>
<td>N/A</td>
</tr>
<tr>
<td>Dolutegravir/Lamivudine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dolutegravir/Rilpivirine</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Juluca</td>
<td>50 mg/25 mg tablet</td>
<td>30 tablets</td>
<td>$2,707</td>
<td>$3,249</td>
<td>N/A</td>
</tr>
<tr>
<td>Doravirine/Tenofovir Disoproxil Fumarate/Lamivudine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delstrigo</td>
<td>100 mg/300 mg/300 mg tablet</td>
<td>30 tablets</td>
<td>$2,100</td>
<td>$2,520</td>
<td>N/A</td>
</tr>
</tbody>
</table>
### Table 19b. Monthly Average Prices of Commonly Used Antiretroviral Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 5 of 5)

<table>
<thead>
<tr>
<th>ARV Drug (Generic and Brand Names)</th>
<th>Strength, Formulation</th>
<th>Tablets, Capsules, or mLs per Month</th>
<th>WAC (Monthly)(^b)</th>
<th>AWP (Monthly)(^b)</th>
<th>FUL (As of Oct. 31, 2019)(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Coformulated Combination Products as Single-Tablet Regimens, continued</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Efavirenz/Tenofovir Disoproxil Fumarate/Emtricitabine</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Atripla</td>
<td>600 mg/300 mg/200 mg tablet</td>
<td>30 tablets</td>
<td>$2,858</td>
<td>$3,429</td>
<td>N/A</td>
</tr>
<tr>
<td>• Symfi 600 mg/300 mg/150 mg tablet</td>
<td>30 tablets</td>
<td>$1,634</td>
<td>$1,961</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>• Symfi Lo 400 mg/300 mg/150 mg tablet</td>
<td>30 tablets</td>
<td>$1,634</td>
<td>$1,961</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td><strong>Elvitegravir/Cobicistat/Tenofovir Alafenamide/Emtricitabine</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Genvoya 150 mg/150 mg/10 mg/200 mg tablet</td>
<td>30 tablets</td>
<td>$3,090</td>
<td>$3,708</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>• Stribild 150 mg/150 mg/300 mg/200 mg tablet</td>
<td>30 tablets</td>
<td>$3,241</td>
<td>$3,889</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td><strong>Rilpivirine/Tenofovir Disoproxil Fumarate/Emtricitabine</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Odefsey 25 mg/25 mg/200 mg tablet</td>
<td>30 tablets</td>
<td>$2,812</td>
<td>$3,375</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>• Complera 25 mg/300 mg/200 mg tablet</td>
<td>30 tablets</td>
<td>$2,812</td>
<td>$3,375</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td><strong>PK Enhancers (Boosters)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cobicistat</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Tybost 150 mg tablet</td>
<td>30 tablets</td>
<td>$230</td>
<td>$277</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td><strong>Ritonavir</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Generic 100 mg tablet</td>
<td>30 tablets</td>
<td>$80 to $222</td>
<td>$278</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Norvir 100 mg tablet</td>
<td>30 tablets</td>
<td>$257</td>
<td>$309</td>
<td>$78</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) The following less commonly used ARV drugs are not included in this table: DLV, ddl, FPV, IDV, NFV, SQV, and d4T.

\(^b\) Source: Micromedex Red Book [database]. IBM Watson Health. 2019. Available at: https://www.micromedexsolutions.com


**Key:** ARV = antiretroviral; AWP = average wholesale price; CD4 = CD4 T lymphocyte; d4t = stavudine; ddl = didanosine; DLV = delavirdine; FPV = fosamprenavir; FUL = federal upper limit; HD = high dose; IDV = indinavir; INSTI = integrase strand transfer inhibitor; N/A = not applicable; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PK = pharmacokinetic; SQV = saquinavir; WAC = wholesale acquisition cost; XR = extended release.

Downloaded from [https://aidsinfo.nih.gov/guidelines](https://aidsinfo.nih.gov/guidelines) on 7/3/2020
Table 20. Mechanisms of Antiretroviral-Associated Drug Interactions (Last updated December 18, 2019; last reviewed December 18, 2019) (page 1 of 2)

PK interactions may occur during absorption, metabolism, or elimination of the ARV drug and/or the interacting drug. 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:** N/A indicates that there are no clinically relevant interactions by the mechanism. Identified mechanisms are specific to the ARV drugs described in the row and may not be reflective of complete ARV regimens. The older PIs FPV, IDV, NFV, and SQV are not commonly used in clinical practice and are not included in this table. Please refer to the FDA product labels for FPV, IDV, NFV, and SQV for information regarding drug interactions with these PIs.

<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>CYP Substrate</th>
<th>CYP Inhibitor</th>
<th>CYP Inducer</th>
<th>UGT1A1</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Increasing Gastric pH</td>
<td>Cationic Chelation</td>
<td>P-gp</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>INSTIs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BIC</td>
<td>N/A</td>
<td>Concentration decreased by products that contain polyvalent cations (e.g., Ca, Mg, Al, Fe, Zn)</td>
<td>Substrate, Inducer, Inhibitor</td>
<td>3A4</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>DTG</td>
<td>N/A</td>
<td>Substrate</td>
<td>3A4 (minor)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>EVG/c</td>
<td>N/A</td>
<td><strong>Inhibitor</strong></td>
<td>3A4</td>
<td>3A4, 2D6</td>
<td>2C9</td>
<td>Substrate</td>
</tr>
<tr>
<td>RAL</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>Substrate</td>
</tr>
<tr>
<td>Pls</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATV</td>
<td>Concentration decreased</td>
<td>N/A</td>
<td>Substrate, Inducer, Inhibitor</td>
<td>3A4</td>
<td>3A4, 2C8</td>
<td>N/A</td>
</tr>
<tr>
<td>ATV/c</td>
<td>N/A</td>
<td>Substrate, effect on P-gp unknown</td>
<td>3A4</td>
<td>3A4, 2D6, 2C8</td>
<td>N/A</td>
<td>No data</td>
</tr>
<tr>
<td>ATV/r</td>
<td>N/A</td>
<td>Substrate, effect on P-gp unknown</td>
<td>3A4</td>
<td>3A4, 2D6</td>
<td>1A2, 2B6, 2C8, 2C9, 2C19</td>
<td>Inducer</td>
</tr>
<tr>
<td>DRV/c</td>
<td>N/A</td>
<td>Substrate</td>
<td>3A4, 2D6</td>
<td>3A4, 2D6</td>
<td>1A2, 2B6, 2C8, 2C9, 2C19</td>
<td>Inducer</td>
</tr>
<tr>
<td>DRV/r</td>
<td>N/A</td>
<td>Substrate, effect on P-gp unknown</td>
<td>3A4, 2D6</td>
<td>1A2, 2B6, 2C8, 2C9, 2C19</td>
<td>Inducer</td>
<td></td>
</tr>
<tr>
<td>TPV/r</td>
<td>N/A</td>
<td>Substrate</td>
<td>3A4, 2D6</td>
<td>3A4, 2D6</td>
<td>No data</td>
<td>Inducer</td>
</tr>
<tr>
<td>NNRTIs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOR</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
<td></td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>EFV</td>
<td>N/A</td>
<td>N/A</td>
<td>2B6 (primary), 2A6, 3A4</td>
<td>3A4</td>
<td>3A4, 2B6, 2C19</td>
<td>N/A</td>
</tr>
<tr>
<td>ETR</td>
<td>N/A</td>
<td>N/A</td>
<td>3A4, 2C9, 2C19</td>
<td>2C9, 2C19</td>
<td>3A4</td>
<td>N/A</td>
</tr>
</tbody>
</table>
Table 20. Mechanisms of Antiretroviral-Associated Drug Interactions  *(Last updated December 18, 2019; last reviewed December 18, 2019)*  (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>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Increasing Gastric pH</td>
<td>Cationic Chelation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NNRTIs, continued</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NVP</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>RPV</td>
<td>Concentration decreased</td>
<td>N/A</td>
</tr>
<tr>
<td>NRTIs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABC</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>FTC</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>3TC</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>TAF</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>TDF</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>ZDV</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>CCR5 Antagonist</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MVC</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Fusion Inhibitor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T-20</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Post-Attachment Inhibitor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IBA</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Key: 3TC = lamivudine; ABC = abacavir; Al = aluminum; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; Ca = calcium; COBI = cobicistat; CYP = cytochrome P; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; Fe = iron; FPV = fosamprenavir; FTC = emtricitabine; IBA = ibalizumab; IDV = indinavir; INSTI = integrase strand transfer inhibitor; LPV/r = lopinavir/ritonavir; Mg = magnesium; MVC = maraviroc; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitors; NVP = nevirapine; P-gp = P-glycoprotein; PK = pharmacokinetic; PI = protease inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQV = saquinavir; T-20 = enfuvirtide; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV/r = tipranavir/ritonavir; UGT = uridine diphosphate glucuronosyltransferase; ZDV = zidovudine; Zn = zinc
Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 1 of 19)

This table provides information on the known or predicted interactions between PIs and non-ARV drugs. When information is available, interactions for boosted ATV (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 for FPV, IDV, NFV, and SQV. For information regarding interactions between PIs and other ARV drugs, including dosing recommendations, refer to Tables 21c, 22a, and 22b.

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 whether 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. In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgement to select the most appropriate alternative medication to use.

Note: FPV, IDV, NFV, and SQV are no longer commonly used in clinical practice and are not included in this table. Please refer to the FDA product labels for FPV, IDV, NFV, and SQV for information regarding drug interactions between these PIs and concomitant medications.

<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>Administer ATV at least 2 hours before or 1–2 hours after antacids or buffered medications.</td>
</tr>
<tr>
<td></td>
<td>TPV/r</td>
<td>TPV AUC ↓ 27%</td>
<td>Administer 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>
</tbody>
</table>
| ATV (unboosted)  | ATPV | When Given Simultaneously with Famotidine:  
• ATV AUC ↓ 41%  
When Given 2 Hours Before and ≥10 Hours After H2RA:  
• ↔ ATV  
A single dose of H2RA 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 twice daily in PI-naive patients.  
Give ATV at least 2 hours before and at least 10 hours after the H2RA.  
**Do not coadminister** unboosted ATV plus H2RA in PI-experienced patients. |
|                  | ATPV | ↓ ATV expected                                   |                                                             |
|                  | ATPV | With Ranitidine:  
• ↔ DRV/r  
←→ PI expected |                                                             |
|                  | ATPV | H2RA dose should not exceed a dose equivalent to famotidine 40 mg twice daily in ART-naive patients or famotidine 20 mg twice daily in ART-experienced patients.  
Give ATV 300 mg (plus COBI 150 mg or RTV 100 mg) simultaneously with and/or ≥10 hours after the dose of H2RA.  
If using TDF and H2RA in ART-experienced patients, use ATV 400 mg (plus COBI 150 mg or RTV 100 mg). |
| **Proton Pump Inhibitors** |     |                                                   |                                             |
| ATPV (unboosted) | ATV | With Omeprazole 40 mg:  
• ATV AUC ↓ 94%  
A single dose of PPI 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.  
**Do not coadminister** in PI-experienced patients. |
| ATV/c, ATV/r     | Omeprazole 40 mg:  
• ATV AUC ↓ 76%  
When Omeprazole 20 mg is Given 12 Hours before ATV/c or ATV/r:  
• ATV AUC ↓ 42%  
A single dose of PPI 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.  
**Do not coadminister** in PI-experienced patients. |

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

Downloaded from https://aidsinfo.nih.gov/guidelines on 7/3/2020
### Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 2 of 19)

<table>
<thead>
<tr>
<th>Acid Reducers, continued</th>
<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>Proton Pump Inhibitors</td>
<td>Acid Reducers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DRV/c, LPV/r</td>
<td>DRV/r</td>
<td>↔ DRV/r</td>
<td>Omeprazole AUC ↓ 42%</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>DRV/r</td>
<td>↔ DRV/r</td>
<td>Omeprazole AUC ↓ 70%</td>
<td>Consider alternative ARV or acid reducer. If coadministered, monitor for omeprazole efficacy. If patient does not experience symptomatic relief, increase dose to no more than omeprazole 40 mg daily.</td>
<td></td>
</tr>
<tr>
<td>TPV/r</td>
<td>↔ TPV/r</td>
<td>Omeprazole AUC ↓ 70%</td>
<td>Do not coadminister.</td>
<td></td>
</tr>
</tbody>
</table>

#### Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia

<table>
<thead>
<tr>
<th>Concomitant Drug</th>
<th>Contraindicated.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alfuzosin</td>
<td>↑ alfuzosin expected</td>
</tr>
<tr>
<td>All PIs</td>
<td>↑ doxazosin possible</td>
</tr>
<tr>
<td>Doxazosin</td>
<td>↑ tamsulosin expected</td>
</tr>
<tr>
<td>Terazosin</td>
<td>↑ silodosin expected</td>
</tr>
</tbody>
</table>

#### Antibacterials

**Antimycobacterials**

<table>
<thead>
<tr>
<th>Concomitant Drug</th>
<th>With LPV/r:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bedaquiline</td>
<td>• Bedaquiline AUC ↑ 1.9-fold</td>
</tr>
<tr>
<td></td>
<td>• Rifabutin AUC ↑ 110% and metabolite AUC ↑ 2,101%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Concomitant Drug</th>
<th>With ATV/r:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifabutin</td>
<td>• Rifabutin AUC ↑ 881%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>With DRV/r:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compared with Rifabutin (300 mg Once Daily) Alone, Rifabutin (150 mg Every Other Day) plus DRV/r:</td>
</tr>
<tr>
<td>• Rifabutin AUC ↑ 203% and metabolite AUC ↑ 375%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>With LPV/r:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compared with Rifabutin (300 mg Once Daily) Alone, Rifabutin (150 mg Once Daily) plus LPV/r:</td>
</tr>
<tr>
<td>• Rifabutin AUC ↑ 190% and metabolite AUC ↑ 1,971%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>With DRV/r, LPV/r:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifabutin (300 mg Once Daily) Alone, Rifabutin (150 mg Once Daily) plus DRV/r, or DRV/c:</td>
</tr>
<tr>
<td>• Rifabutin AUC ↑ 110% and metabolite AUC ↑ 2,101%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>With DRV/r, LPV/r:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifabutin (300 mg Once Daily) Alone, Rifabutin (150 mg Once Daily) plus DRV/r, or DRV/c:</td>
</tr>
<tr>
<td>• Rifabutin AUC ↑ 110% and metabolite AUC ↑ 2,101%</td>
</tr>
</tbody>
</table>

**Rifabutin**

<table>
<thead>
<tr>
<th>Concomitant Drug</th>
<th>Rifabutin AUC ↑ 163% and metabolite AUC ↑ 1,175%</th>
</tr>
</thead>
</table>

**Rifabutin (unboosted)**

<table>
<thead>
<tr>
<th>Concomitant Drug</th>
<th>Rifabutin AUC ↑ 163% and metabolite AUC ↑ 1,175%</th>
</tr>
</thead>
</table>

**Do not coadminister, unless benefits outweigh risks.** Monitor liver function and ECG for QTc prolongation.

PK data in this table are results from healthy volunteer studies. Lower rifabutin exposure has been reported in patients with HIV than in healthy study participants.

**Do not coadminister.**

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

Downloaded from https://aidsinfo.nih.gov/guidelines on 7/3/2020
### Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs  (Last updated December 18, 2019; last reviewed December 18, 2019) (page 3 of 19)

<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>Antibacterials</strong>, continued</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rifampin</td>
<td>All PIs</td>
<td>↓ PI concentration by &gt;75%</td>
<td><strong>Contraindicated.</strong> Increasing the dose of RTV does not overcome this interaction and may increase hepatotoxicity. Increasing the COBI dose is not recommended. Consider rifabutin if a rifamycin is indicated.</td>
</tr>
<tr>
<td><strong>Antimycobacterials</strong>, continued</td>
<td></td>
<td></td>
<td></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>Macrolides</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Azithromycin</strong></td>
<td>ATV (unboosted), ATV/c, ATV/r</td>
<td>↑ azithromycin possible</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>DRV/c, DRV/r, TPV/r</td>
<td>↔ azithromycin expected</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PI/c, PI/r</td>
<td>Clarithromycin AUC ↑ 94%</td>
<td>Reduce clarithromycin dose by 50% or consider alternative ARV or azithromycin. Monitor for clarithromycin-related adverse events, including QTc prolongation.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DRV/r ↑ clarithromycin AUC 57%</td>
<td>If use of clarithromycin is necessary in a patient with impaired renal function, reduce clarithromycin dose by 50% in patients with CrCl 30 to 60 mL/min. In patients with CrCl &lt;30 mL/min, reduce clarithromycin dose by 75%.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LPV/r ↑ clarithromycin expected</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>RTV 500 mg twice daily ↑ clarithromycin 77%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TPV/r ↑ clarithromycin 19%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clarithromycin ↑ TPV 66%</td>
<td></td>
</tr>
<tr>
<td><strong>Erythromycin</strong></td>
<td>All PIs</td>
<td>↑ erythromycin expected</td>
<td>Consider alternative ARV or use azithromycin.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ PIs expected</td>
<td></td>
</tr>
<tr>
<td><strong>Anticoagulants</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apixaban</td>
<td>ATV (unboosted)</td>
<td>No data</td>
<td><strong>No data available for dose recommendation. Consider alternative ARV or anticoagulant:</strong></td>
</tr>
<tr>
<td></td>
<td>PI/c, PI/r</td>
<td>↑ apixaban expected</td>
<td><strong>Do not coadminister</strong> in patients who require apixaban 2.5 mg twice daily.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Betrixaban</td>
<td>ATV (unboosted)</td>
<td>No data</td>
<td><strong>No data available for dose recommendation. Consider alternative ARV or anticoagulant:</strong></td>
</tr>
<tr>
<td></td>
<td>ATV/c, ATV/r, LPV/r</td>
<td>↑ betrixaban expected</td>
<td>Administer an initial single dose of betrixaban 80 mg followed by betrixaban 40 mg once daily.</td>
</tr>
<tr>
<td></td>
<td>DRV/c, DRV/r, TPV/r</td>
<td>No data</td>
<td><strong>No data available for dose recommendation. Consider alternative ARV or anticoagulant:</strong></td>
</tr>
<tr>
<td>Dabigatran</td>
<td>ATV (unboosted)</td>
<td>No data</td>
<td><strong>No data available for dose recommendation. Consider alternative ARV or anticoagulant:</strong></td>
</tr>
<tr>
<td></td>
<td>ATV/c, ATV/r, LPV/r</td>
<td>↑ dabigatran expected</td>
<td>Dabigatran dosing recommendation depends on indication and renal function. Refer to dabigatran prescribing information for dosing instructions when using dabigatran concomitantly with P-glycoprotein inhibitors.</td>
</tr>
<tr>
<td></td>
<td>With COBI 150 mg Alone:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Dabigatran AUC ↑ 110% to 127%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>DRV/c, DRV/r, TPV/r</td>
<td>No data</td>
<td><strong>No data available for dose recommendation. Consider alternative ARV or anticoagulant:</strong></td>
</tr>
</tbody>
</table>
### Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019)

<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>Anticoagulants</strong>, continued</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Edoxaban</td>
<td>ATV (unboosted)</td>
<td>No data</td>
<td>No data available for dose recommendation. Consider alternative ARV or anticoagulant.</td>
</tr>
</tbody>
</table>
| | ATV/c, ATV/r, LPV/r | ↑ edoxaban expected | Stroke Prevention in Nonvalvular Atrial Fibrillation Indication:  
• No dose adjustment needed. |
| | | | Deep Venous Thrombosis and Pulmonary Embolism Indication:  
• Administer edoxaban 30 mg once daily. |
| | DRV/c, DRV/r, TPV/r | No data | No data available for dose recommendation. Consider alternative ARV or anticoagulant. |
| Rivaroxaban | ATV (unboosted) | No data | No data available for dose recommendation. Consider alternative ARV or anticoagulant. |
| | PI/c, PI/r | ↑ rivaroxaban expected | Do not coadminister. |
| Warfarin | PI/c | No data | Monitor INR closely when stopping or starting PI/c or PI/r and adjust warfarin dose accordingly. |
| | PI/r | ↓ warfarin possible | If switching between RTV and COBI, the effect of COBI on warfarin is not expected to be equivalent to RTV's effect on warfarin. |
| **Anticonvulsants** | | | |
| Carbamazepine | ATV (unboosted) | May ↓ PI concentrations substantially | Do not coadminister. |
| | ATV/r, LPV/r, TPV/r | ↑ carbamazepine possible  
TPV/r ↑ carbamazepine AUC 26%  
May ↓ PI concentrations substantially | Consider alternative ARV or anticonvulsant. If coadministration is necessary, consider monitoring concentrations of both drugs and assess virologic response.  
**Do not coadminister with LPV/r once daily.** |
| | DRV/r | Carbamazepine AUC ↑ 45%  
↔ DRV | Monitor anticonvulsant concentration and adjust dose accordingly. |
| | PI/c | ↑ carbamazepine possible  
↓ cobicistat expected  
↓ PI expected | Contraindicated. |
| Eslicarbazepine | All PIs | ↓ PI possible | Consider alternative ARV or anticonvulsant. If coadministration is necessary, monitor for virologic response. Consider monitoring anticonvulsant and PI concentrations. |
| Ethosuximide | All PIs | ↑ ethosuximide possible | Monitor for ethosuximide-related adverse events. |
| Lamotrigine | ATV (unboosted) | ↔ lamotrigine | No dose adjustment needed. |
| | ATV/r | Lamotrigine AUC ↓ 32%  
↔ LPV | A dose increase of lamotrigine may be needed; monitor lamotrigine concentration or consider alternative ARV or anticonvulsant. |
| | LPV/r | Lamotrigine AUC ↓ 50%  
↔ LPV | |
| | DRV/r, TPV/r | ↓ lamotrigine possible | |
| | PI/c | No data | Monitor anticonvulsant concentration and adjust dose accordingly. |
## Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs  (Last updated December 18, 2019; last reviewed December 18, 2019)  (page 5 of 19)

<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>Oxcarbazepine</td>
<td>All PIs</td>
<td>↓ PI possible</td>
<td>Consider alternative ARV or anticonvulsant. If coadministration is necessary, monitor for virologic response. Consider monitoring anticonvulsant and PI concentrations.</td>
</tr>
<tr>
<td></td>
<td>ATV (unboosted)</td>
<td>↓ ATV expected</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td>ATP/DRV/TPV</td>
<td>↓ phenytoin possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ PI possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LPV/r</td>
<td>↓ phenytoin possible</td>
<td>Do not coadminister with LPV/r once daily.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ LPV/r possible</td>
<td>Consider alternative anticonvulsant. If coadministration is necessary, consider monitoring concentrations of both drugs and assessing virologic response.</td>
</tr>
<tr>
<td></td>
<td>Pl/c</td>
<td>↓ cobicistat expected</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ PI expected</td>
<td></td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>ATV (unboosted)</td>
<td>↓ ATV expected</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td>ATP/DRV/TPV</td>
<td>↓ phenytoin possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ PI possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LPV/r</td>
<td>Phenytoin AUC ↓ 31%</td>
<td>Do not coadminister with LPV/r once daily.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LPV/r AUC ↓ 33%</td>
<td>Consider alternative anticonvulsant or monitor concentrations of both drugs and assess virologic response.</td>
</tr>
<tr>
<td></td>
<td>Pl/c</td>
<td>↓ cobicistat expected</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ PI expected</td>
<td></td>
</tr>
<tr>
<td>Valproic Acid</td>
<td>All PIs</td>
<td>↓ or ↔ VPA possible</td>
<td>Monitor VPA concentrations and monitor for PI tolerability.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LPV AUC ↑ 38%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>No data for other PIs</td>
<td></td>
</tr>
<tr>
<td><strong>Antidepressants, Anxiolytics, and Antipsychotics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bupropion</td>
<td>ATV/DRV</td>
<td>↓ bupropion possible</td>
<td>Titrate bupropion dose based on clinical response.</td>
</tr>
<tr>
<td></td>
<td>TPV</td>
<td>Bupropion AUC ↓ 46%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LPV/r</td>
<td>Bupropion AUC ↓ 57%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pl/c</td>
<td>↔ bupropion expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>Buspirone</td>
<td>All PIs</td>
<td>↑ buspirone expected</td>
<td>Administer lowest dose of buspirone with caution and titrate buspirone dose based on clinical response.</td>
</tr>
<tr>
<td>Nefazodone</td>
<td>All PIs</td>
<td>↑ nefazodone expected</td>
<td>Monitor for nefazodone-related adverse events and PI tolerability.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ PI possible</td>
<td></td>
</tr>
<tr>
<td>Trazodone</td>
<td>All PIs</td>
<td>RTV 200 mg twice daily (for 2 days)</td>
<td>Administer lowest dose of trazodone and monitor for CNS and CV adverse events.</td>
</tr>
<tr>
<td>Concomitant Drug</td>
<td>PI</td>
<td>Effect on PI 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>Antidepressants, Anxiolytics, and Antipsychotics, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Tricyclic Antidepressants</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amitriptyline, amoxapine, clomipramine, desipramine, doxepin, imipramine, maprotiline, nortriptyline, protriptyline, trimipramine</td>
<td>All PIs</td>
<td>↑ TCA expected</td>
<td>Administer lowest possible TCA dose and titrate based on clinical assessment and/or drug concentrations.</td>
</tr>
<tr>
<td>Selective Serotonin Reuptake Inhibitors (e.g., citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline)</td>
<td>DRV/r</td>
<td>Paroxetine AUC ↓ 39% Sertraline AUC ↓ 49%</td>
<td>Titrate SSRI dose based on clinical response.</td>
</tr>
<tr>
<td></td>
<td>All PIs except DRV/r</td>
<td>No data</td>
<td>Titrate SSRI dose using the lowest available initial or maintenance dose.</td>
</tr>
<tr>
<td><strong>Antipsychotics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>PI/c, PI/r</td>
<td>↑ aripiprazole expected</td>
<td>Administer 25% of the usual aripiprazole dose. Titrate dose based on clinical monitoring for efficacy/adverse events. Refer to aripiprazole label for doses to use in patients who have major depressive disorder or who are known to be CYP2D6 poor metabolizers.</td>
</tr>
<tr>
<td></td>
<td>ATV (unboosted)</td>
<td>↑ aripiprazole expected</td>
<td>Administer 50% of the usual aripiprazole dose. Titrate dose based on clinical monitoring for efficacy/adverse events. Refer to aripiprazole label for doses to use in patients who have major depressive disorder or who are known to be CYP2D6 poor metabolizers.</td>
</tr>
<tr>
<td>Brexpiprazole</td>
<td>PI/c, PI/r</td>
<td>↑ brexpiprazole expected</td>
<td>Administer 25% of the usual brexpiprazole dose. Titrate dose based on clinical monitoring for efficacy/adverse events. Refer to brexpiprazole label for doses to use in patients who have major depressive disorder or who are known to be CYP2D6 poor metabolizers.</td>
</tr>
<tr>
<td></td>
<td>ATV (unboosted)</td>
<td>↑ brexpiprazole expected</td>
<td>Administer 50% of the usual brexpiprazole dose. Titrate dose based on clinical monitoring for efficacy/adverse events. Refer to brexpiprazole label for doses to use in patients who have major depressive disorder or who are known to be CYP2D6 poor metabolizers.</td>
</tr>
<tr>
<td>Cariprazine</td>
<td>All PIs</td>
<td>↑ cariprazine expected</td>
<td><strong>Starting Cariprazine in a Patient Who Is Already Receiving a PI:</strong>&lt;br&gt;• Administer cariprazine 1.5 mg on Day 1 and Day 3, with no dose given on Day 2. From Day 4 onward, administer cariprazine 1.5 mg daily. Dose can be increased to a maximum dose of cariprazine 3 mg daily. If the PI is withdrawn, cariprazine dose may need to be increased.</td>
</tr>
</tbody>
</table>

---

*Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV*
Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs  *(Last updated December 18, 2019; last reviewed December 18, 2019)*  (page 7 of 19)

Also see Sedative/Hypnotics section below

<table>
<thead>
<tr>
<th>Antidepressants, Anxiolytics, and Antipsychotics, continued</th>
<th>Effect on PI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Iloperidone</strong></td>
<td>↑ iloperidone expected</td>
<td>Decrease iloperidone dose by 50%.</td>
</tr>
<tr>
<td><strong>Lurasidone</strong></td>
<td>↑ lurasidone expected</td>
<td>Consider alternative ARV or antipsychotic.</td>
</tr>
<tr>
<td></td>
<td>↑ antipsychotic possible</td>
<td>If coadministration is necessary, reduce lurasidone dose by 50%.</td>
</tr>
<tr>
<td></td>
<td>Contraindicated.</td>
<td></td>
</tr>
<tr>
<td><strong>Other Antipsychotics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CYP3A4 and/or CYP2D6 substrates (e.g., clozapine, perphenazine, risperidone, thioridazine)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>↑ antipsychotic possible</td>
<td>Titrating antipsychotic dose using the lowest initial dose or adjust maintenance dose accordingly. Monitor for adverse events, including QTc prolongation.</td>
</tr>
<tr>
<td></td>
<td>Contraindicated.</td>
<td></td>
</tr>
<tr>
<td><strong>Pimavanserin</strong></td>
<td>↑ pimavanserin expected</td>
<td>Do not coadminister; due to risk for QTc prolongation.</td>
</tr>
<tr>
<td></td>
<td>No data</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Do not coadminister; due to risk for QTc prolongation.</td>
<td></td>
</tr>
<tr>
<td><strong>Pimozide</strong></td>
<td>↑ pimozide expected</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Quetiapine</strong></td>
<td>↑ quetiapine expected</td>
<td>Starting Quetiapine in a Patient Receiving a PI:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Initiate quetiapine at the lowest dose and titrate up as needed. Monitor for quetiapine effectiveness and adverse events.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Starting a PI in a Patient Receiving a Stable Dose of Quetiapine:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Reduce quetiapine dose to 1/6 of the current dose. Closely monitor for quetiapine effectiveness and adverse events.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>↑ ziprasidone expected</td>
<td>Do not coadminister; due to risk for QTc prolongation.</td>
</tr>
<tr>
<td></td>
<td>All PIs except LPV/r</td>
<td>Monitor for ziprasidone-related adverse events.</td>
</tr>
<tr>
<td></td>
<td>LPV/r</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Isavuconazole AUC ↑ 96%</td>
<td>If coadministered, monitor isavuconazole concentrations and adverse events. Monitor for virologic response.</td>
</tr>
<tr>
<td></td>
<td>LPV AUC ↓ 27%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RTV AUC ↓ 31%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>↑ or ↓ PI possible</td>
<td>If coadministered, monitor isavuconazole concentrations and monitor for isavuconazole-related adverse events. Monitor for PI tolerability and virologic response.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>↑ itraconazole expected</td>
<td>Itraconazole doses &gt;200 mg/day are not recommended with PI/r, ATV/c, or DRV/c unless dosing is guided by itraconazole concentrations.</td>
</tr>
<tr>
<td></td>
<td>All PIs</td>
<td></td>
</tr>
</tbody>
</table>
Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs  *(Last updated December 18, 2019; last reviewed December 18, 2019)* (page 8 of 19)

<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</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Posaconazole</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| ATV              | ATV | ATV AUC ↑ 268%  
↑ posaconazole possible  | If coadministered, monitor posaconazole concentrations and monitor for posaconazole-related or PI-related adverse events. |
| ATV/r            | ATV | ATV AUC ↑ 146%  
↑ posaconazole possible  |                                             |
| All other PIs    | ATV | ↑ PI possible  
↑ posaconazole possible  | If coadministered, monitor postaconazole concentrations and monitor for posaconazole-related or PI-related adverse events. |
| **Voriconazole** |    |                                               |                                             |
| ATV (unboosted)  | ATV | ↑ PI possible  
↑ voriconazole possible  | If coadministered, monitor voriconazole concentrations and monitor for voriconazole-related or PI-related adverse events. |
| PI/c             | ATV | ↑ PI possible  
↑ voriconazole possible  | Do not coadminister voriconazole and RTV or COBI unless benefits outweigh risks. If coadministered, monitor voriconazole concentration and adjust dose accordingly. |
| PI/r             | ATV | RTV 100 mg twice daily ↓  
voriconazole AUC 39%  |                                             |

| **Antimalarials** |    |                                               |                                             |
| **Artemether/ Lumefantrine** |    |                                               |                                             |
| ATV (unboosted), PI/c |    | ↑ lumefantrine expected  
No data for artemether  | Clinical significance unknown. If coadministered, monitor closely for antimalarial efficacy and lumefantrine toxicity, including QTc prolongation. |
| DRV/r             |    | Artemether AUC ↓ 16%  
DHA AUC ↓ 18%  
Lumefantrine AUC ↑ 175%  
↔ DRV  |                                             |
| LPV/r             |    | Artemether AUC ↓ 40%  
DHA AUC ↓ 45%  
Lumefantrine AUC ↑ 4.8-fold  
↔ LPV  |                                             |
| TPV/r             |    | ↑ lumefantrine expected  | Do not coadminister, due to risk for QTc prolongation. |

| **Atovaquone/Proguanil** |    |                                               |                                             |
| ATV/r, LPV/r       |    | With ATV/r:  
• Atovaquone AUC ↓ 46%  
• Proguanil AUC ↓ 41%  | Clinical significance unknown. Consider alternative ARV or malaria prophylaxis. |
|                    |    | With LPV/r:  
• Atovaquone AUC ↓ 74%  
• Proguanil AUC ↓ 38%  |                                             |
|                    |    | With ATV (unboosted), PI/c, or PI/r:  
• No data  
• ↑ mefloquine possible  |                                             |

| **Mefloquine**     |    |                                               |                                             |
| All PIs            |    | With RTV 200 mg Twice Daily:  
• RTV AUC ↓ 31% and C min ↓ 43%  
• ↔ mefloquine  | Clinical significance unknown. Consider alternative ARV or antimalarial drug. If coadministered, monitor for mefloquine-related adverse events, including psychiatric symptoms and QTc prolongation. Monitor virologic response. |
|                    |    | With ATV (unboosted), PI/c, or PI/r:  
• No data  
• ↑ mefloquine possible  |                                             |
### Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs  *(Last updated December 18, 2019; last reviewed December 18, 2019)*  
*(page 9 of 19)*

<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>Antiplatelets</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>All PIs</td>
<td>Clopidogrel active metabolite AUC ↓ 320% with impaired platelet inhibition</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td>Prasugrel</td>
<td>All PIs</td>
<td>Prasugrel active metabolite AUC ↓ 210% with adequate platelet inhibition</td>
<td>Insufficient data to make a recommendation.</td>
</tr>
<tr>
<td>Ticagrelor</td>
<td>All PIs</td>
<td>↑ ticagrelor expected</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td>Vorapaxar</td>
<td>All PIs</td>
<td>↑ vorapaxar expected</td>
<td>Do not coadminister.</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 needed.</td>
</tr>
<tr>
<td>Oral suspension</td>
<td>All other PIs</td>
<td>↔ atovaquone expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td><strong>Beta-Agonists, Long-Acting Inhaled</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arformoterol, Formoterol</td>
<td>ATV (unboosted), ATPV/c, ATV/r</td>
<td>↑ arformoterol possible</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>DRV/c, DRV/r, LPV/r, TPV/r</td>
<td>↔ arformoterol expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>Indacaterol</td>
<td>All PIs</td>
<td>With RTV 300 mg Twice Daily: ↑ Indacaterol AUC ↑ 1.7-fold</td>
<td>No dose adjustment needed in patients receiving indacaterol 75 mcg daily.</td>
</tr>
<tr>
<td>Olodaterol</td>
<td>All PIs</td>
<td>↑ olodaterol expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>Salmeterol</td>
<td>All PIs</td>
<td>↑ salmeterol possible</td>
<td>Do not coadminister, due to potential increased risk of salmeterol-associated CV events.</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>↑ amiodarone possible</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td></td>
<td>All other PIs</td>
<td>↑ amiodarone possible</td>
<td>Do not coadminister unless benefits outweigh risks. If coadministered, monitor for amiodarone-related adverse events and consider monitoring ECG and amiodarone drug concentration.</td>
</tr>
<tr>
<td>Antiarrhythmics (e.g., disopyramide, dofetilide, lidocaine, mexiletine, propafenone)</td>
<td>ATV (unboosted)</td>
<td>↑ antiarrhythmic possible</td>
<td>Consider alternative ARV or antiarrhythmics. If coadministered, monitor for antiarrhythmic toxicities.</td>
</tr>
<tr>
<td></td>
<td>PI/c, PI/r</td>
<td>↑ antiarrhythmic possible</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td>Dronedarone</td>
<td>ATPV (unboosted)</td>
<td>↑ dronedarone possible</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td>PI/c, PI/r</td>
<td>↑ dronedarone expected</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td>Flecainide</td>
<td>All PIs except TPV/r</td>
<td>↑ flecainide possible</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td>TPV/r</td>
<td>↑ flecainide expected</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td>Propafenone</td>
<td>All PIs except TPV/r</td>
<td>↑ propafenone possible</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td>TPV/r</td>
<td>↑ propafenone expected</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td>Quinidine</td>
<td>All PIs except TPV/r</td>
<td>↑ quinidine possible</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td>TPV/r</td>
<td>↑ quinidine expected</td>
<td>Contraindicated.</td>
</tr>
</tbody>
</table>
### Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 10 of 19)

<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>
<tr>
<td><strong>Beta-Blockers</strong> (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>
<tr>
<td><strong>Bosentan</strong></td>
<td>All PIs</td>
<td>With LPV/r:</td>
<td>Do not coadminister bosentan and unboosted ATV.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• ↑ bosentan 48-fold (Day 4) and ↑ 5-fold (Day 10)</td>
<td>In Patients on a PI (Other than Unboosted ATV) &gt;10 Days:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ ATV expected</td>
<td>• Start bosentan at 62.5 mg once daily or every other day.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>In Patients on Bosentan who Require a PI (Other than Unboosted ATV):</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• 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.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>When Switching Between COBI and RTV:</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Maintain same bosentan dose.</td>
</tr>
<tr>
<td><strong>Calcium Channel Blockers, Except Diltiazem</strong></td>
<td>All PIs</td>
<td>↑ dihydropyridine possible</td>
<td>Titrate CCB dose and monitor closely. ECG monitoring is recommended when CCB is used with ATV.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ verapamil possible</td>
<td></td>
</tr>
<tr>
<td><strong>Digoxin</strong></td>
<td>PI/c, PI/r</td>
<td>RTV 200 mg twice daily ↑ digoxin AUC 29% and ↑ half-life 43%</td>
<td>Monitor digoxin concentrations. Digoxin dose may need to be decreased. Titrate initial digoxin dose.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DRV/r ↑ digoxin AUC 36%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>COBI ↑ digoxin C&lt;sub&gt;max&lt;/sub&gt; 41% and ↔ AUC</td>
<td></td>
</tr>
<tr>
<td><strong>Diltiazem</strong></td>
<td>ATV (unboosted), ATV/c, ATV/r</td>
<td>Unboosted ATV ↑ diltiazem AUC 125%</td>
<td>Decrease diltiazem dose by 50%. ECG monitoring is recommended.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Greater ↑ likely with ATV/c or ATV/r</td>
<td></td>
</tr>
<tr>
<td></td>
<td>DRV/c, DRV/r, LPV/r, TPV/r</td>
<td>↑ diltiazem possible</td>
<td>Titrate diltiazem dose according to clinical response and toxicities.</td>
</tr>
<tr>
<td><strong>Eplerenone</strong></td>
<td>PI/c, PI/r</td>
<td>↑ eplerenone expected</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td><strong>Ranolazine</strong></td>
<td>ATV (unboosted)</td>
<td>↑ ranolazine possible</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>PI/c, PI/r</td>
<td>↑ ranolazine expected</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td><strong>Ivabradine</strong></td>
<td>All PIs</td>
<td>↑ ivabradine expected</td>
<td></td>
</tr>
<tr>
<td><strong>Corticosteroids</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Beclomethasone</strong> Inhaled or intranasal</td>
<td>DRV/r</td>
<td>↔ 17-BMP (active metabolite) AUC</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RTV 100 mg twice daily ↑ 17-BMP AUC 2-fold</td>
<td></td>
</tr>
<tr>
<td></td>
<td>All PIs except DRV/r</td>
<td>↔ 17-BMP expected</td>
<td></td>
</tr>
</tbody>
</table>
### Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs *(Last updated December 18, 2019; last reviewed December 18, 2019)* (page 11 of 19)

<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>Budesonide, Ciclesonide, Fluticasone, Mometasone</td>
<td>All PIs</td>
<td>↑ glucocorticoids possible&lt;br&gt;RTV 100 mg twice daily ↑ fluticasone AUC 350-fold</td>
<td>Do not coadminister unless potential benefits of inhaled or intranasal corticosteroid outweigh the risks of adverse events associated with corticosteroids. Coadministration can result in adrenal insufficiency and Cushing’s syndrome. Consider alternative inhaled/intranasal corticosteroid (e.g., beclomethasone).</td>
</tr>
<tr>
<td><strong>Betamethasone, Budesonide</strong>&lt;br&gt;Systemic</td>
<td>All PIs</td>
<td>↑ glucocorticoids possible&lt;br&gt;↓ PI possible</td>
<td>Do not coadminister unless potential benefits of systemic corticosteroid outweigh the risks of adverse events associated with systemic corticosteroids. Coadministration can result in adrenal insufficiency and Cushing’s syndrome.</td>
</tr>
<tr>
<td><strong>Dexamethasone</strong>&lt;br&gt;Systemic</td>
<td>All PIs</td>
<td>↑ glucocorticoids possible&lt;br&gt;↓ PI possible</td>
<td>Consider alternative corticosteroid for long-term use. If coadministration is necessary, monitor virologic response to ART.</td>
</tr>
<tr>
<td><strong>Prednisone, Prednisolone</strong>&lt;br&gt;Systemic</td>
<td>LPV/r</td>
<td>↑ prednisolone AUC 31%</td>
<td>Coadministration may be considered if the potential benefits outweigh the risks of adverse events associated with systemic corticosteroids. If coadministered, monitor for adrenal insufficiency, Cushing’s syndrome, and other corticosteroid-associated toxicities.</td>
</tr>
<tr>
<td><strong>Betamethasone, Methylprednisolone, Triamcinolone</strong>&lt;br&gt;Local injections, including intra-articular, epidural, or intra-orbital</td>
<td>All PIs</td>
<td>↑ glucocorticoids expected</td>
<td>Do not coadminister. Coadministration can result in adrenal insufficiency and Cushing’s syndrome.</td>
</tr>
</tbody>
</table>

#### Glucose-Lowering Medications

<table>
<thead>
<tr>
<th>Glucose-Lowering Medications</th>
<th>PI/rt</th>
<th>Effect on PI or coadministration</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Canagliflozin</strong>&lt;br&gt;ATV (unboosted), PI/c</td>
<td></td>
<td>↔ canagliflozin</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td><strong>Pi/rt</strong></td>
<td></td>
<td>↓ canagliflozin expected</td>
<td>If a patient is already tolerating canagliflozin 100 mg daily, increase canagliflozin dose to 200 mg daily. &lt;br&gt; If a patient is already tolerating canagliflozin 200 mg daily and requires additional glycemic control, management strategy is based on renal function. &lt;br&gt; In Patients with eGFR ≥60 mL/min/1.73 m²: &lt;br&gt; • Canagliflozin dose may be increased to 300 mg daily. &lt;br&gt; In Patients with eGFR &lt;60 mL/min/1.73 m²: &lt;br&gt; • Consider adding another antihyperglycemic agent.</td>
</tr>
<tr>
<td><strong>Saxagliptin</strong></td>
<td>All PIs</td>
<td>↑ saxagliptin expected</td>
<td>Limit saxagliptin dose to 2.5 mg once daily.</td>
</tr>
<tr>
<td><strong>Dapagliflozin/Saxagliptin</strong></td>
<td>All PIs</td>
<td>↑ saxagliptin expected</td>
<td>Do not coadminister. Dapagliflozin is only available as a coformulated drug that contains 5 mg of saxagliptin. When coadministered with EVG/c, the dose of saxagliptin should not exceed 2.5 mg once daily; thus, this combination is not recommended.</td>
</tr>
</tbody>
</table>
### Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs *(Last updated December 18, 2019; last reviewed December 18, 2019)* (page 12 of 19)

<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>Hepatitis C Direct-Acting Antiviral Agents</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<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 needed.</td>
</tr>
<tr>
<td></td>
<td>TPV/r</td>
<td>No data</td>
<td>No data available for dose recommendation.</td>
</tr>
<tr>
<td><strong>Dasabuvir plus Paritaprevir/Ombitasvir/RTV</strong></td>
<td>ATV (unboosted)</td>
<td>↔ ATV</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ATV/c, ATV/r</td>
<td>No data</td>
<td></td>
</tr>
<tr>
<td></td>
<td>DRV DRV Cmin ↓ 43% to 48%</td>
<td>Do not coadminister.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LPV/r</td>
<td>Paritaprevir AUC ↑ 117%</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td>DRV/c, TPV/r</td>
<td>No data</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td>Elbasvir/Grazoprevir</td>
<td>ATV/r</td>
<td>Elbasvir AUC ↑ 4.8-fold&lt;br&gt;Grazoprevir AUC ↑ 10.6-fold&lt;br&gt;Elbasvir ↔ ATV&lt;br&gt;Grazoprevir ↑ ATV AUC 43%</td>
<td>Contraindicated.&lt;br&gt;May increase the risk of ALT elevations due to a significant increase in grazoprevir plasma concentrations caused by OATP1B1/3 inhibition.</td>
</tr>
<tr>
<td></td>
<td>DRV/r</td>
<td>Elbasvir AUC ↑ 66%&lt;br&gt;Grazoprevir AUC ↑ 7.5-fold&lt;br&gt;↔ DRV</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LPV/r</td>
<td>Elbasvir AUC ↑ 3.7-fold&lt;br&gt;Grazoprevir AUC ↑ 12.9-fold&lt;br&gt;↔ LPV</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ATV (unboosted), ATV/c, DRV/c, TPV/r</td>
<td>↑ grazoprevir expected</td>
<td></td>
</tr>
<tr>
<td>Concomitant Drug</td>
<td>PI</td>
<td>Effect on PI and/or Concomitant Drug Concentrations</td>
<td>Dosing Recommendations and Clinical Comments</td>
</tr>
<tr>
<td>------------------</td>
<td>----</td>
<td>---------------------------------------------------</td>
<td>---------------------------------------------</td>
</tr>
</tbody>
</table>
| **Glecaprevir/Pibrentasvir** | **ATV (unboosted), ATV/c, ATV/r** | With (ATV 300 mg plus RTV 100 mg) Once Daily:  
• Glecaprevir AUC ↑ 6.5-fold  
• Pibrentasvir AUC ↑ 64% | Contraindicated. |
| | **DRV/c, DRV/r** | With (DRV 800 mg plus RTV 100 mg) Once Daily:  
• Glecaprevir AUC ↑ 5-fold  
• ↔ pibrentasvir | Do not coadminister. |
| | **LPV/r** | Glecaprevir AUC ↑ 4-fold  
Pibrentasvir ↑ 2.5-fold | Do not coadminister. |
| | **TPV/r** | ↑ glecaprevir and pibrentasvir expected | Do not coadminister. |
| **Ledipasvir/Sofosbuvir** | **ATV/r** | ATV AUC ↑ 33%  
Ledipasvir AUC ↑ 113%  
↔ sofosbuvir | No dose adjustment needed.  
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 risk of TDF toxicities. If coadministration is necessary, monitor for TDF-associated adverse reactions. |
| | **ATV (unboosted), ATV/c, DRV/c, DRV/r, LPV/r** | ↔ PI expected  
↔ ledipasvir and sofosbuvir | No dose adjustment needed. |
| | **TPV/r** | ↓ ledipasvir and sofosbuvir expected | Do not coadminister. |
| **Sofosbuvir/Velpatasvir** | **ATV/r** | ↔ ATV/r  
↔ sofosbuvir  
Velpatasvir AUC ↑ 2.4-fold | No dose adjustment needed. |
| | **DRV/r** | ↔ DRV/r  
Sofosbuvir AUC ↓ 28%  
↔ velpatasvir | No dose adjustment needed. |
| | **ATV (unboosted), ATV/c, DRV/c, LPV/r** | ↔ sofosbuvir and velpatasvir expected | No dose adjustment needed. |
| | **TPV/r** | ↓ sofosbuvir expected  
↓ velpatasvir expected | Do not coadminister. |
| **Sofosbuvir/Velpatasvir/Voxilaprevir** | **ATV (unboosted), ATV/c, ATV/r** | With ATV/r:  
• Voxilaprevir AUC ↑ 4.3-fold  
• Velpatasvir AUC ↑ 93%  
• Sofosbuvir AUC ↑ 40% | Do not coadminister. |
| | **LPV/r** | ↑ voxilaprevir expected | Do not coadminister. |
| | **DRV/c, DRV/r** | With DRV/r:  
• Voxilaprevir AUC ↑ 2.4-fold  
• ↔ DRV/r, velpatasvir, and sofosbuvir | No dose adjustment needed. |
<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>Hepatitis C Direct-Acting Antiviral Agents, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir/Velpatasvir/</td>
<td>TPV/r</td>
<td>↓ sofosbuvir expected</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td>Voxilaprevir, continued</td>
<td></td>
<td>↓ velpatasvir expected</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Effect on voxilaprevir is unknown.</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>All PIs</td>
<td>↓ PI expected</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td><strong>Hormonal Therapies</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contraceptives – Injectable Depot MPA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Herbal Products</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Contraceptives – Oral</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATV (unboosted)</td>
<td>LPV/r</td>
<td>Ethinyl estradiol AUC ↑ 48%</td>
<td>Contraindicated with drospirenone-containing hormonal contraceptive due to potential for hyperkalemia. Use alternative ARV or contraceptive methods.</td>
</tr>
<tr>
<td></td>
<td>All other PIs</td>
<td>MPA AUC ↑ 46% and ↔ Cmin</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ethinyl estradiol AUC ↓ 22%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>↔ ethinyl estradiol AUC and Cmin ↓ 25%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>↔ levonorgestrel</td>
<td></td>
</tr>
<tr>
<td>ATV/r</td>
<td></td>
<td>Ethinyl estradiol AUC ↓ 19% and Cmin ↓ 37%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Norgestimate AUC ↑ 85%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Norethindrone AUC ↑ 51% and Cmin ↑ 67%</td>
<td></td>
</tr>
<tr>
<td>DRV/c</td>
<td></td>
<td>Drosperone AUC ↑ 1.6-fold</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ethinyl estradiol AUC ↓ 30%</td>
<td></td>
</tr>
<tr>
<td>DRV/r, LPV/r,</td>
<td></td>
<td>Ethinyl estradiol AUC ↓ 37% to 55%</td>
<td></td>
</tr>
<tr>
<td>TPV/r</td>
<td></td>
<td>Norethindrone AUC ↓ 14% to 34%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>With TPV/r:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• ↔ norethindrone AUC</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contraceptives – Subdermal Implant Etonogestrel</td>
<td>LPV/r</td>
<td>Etonogestrel AUC ↑ 52% and Cmin ↑ 34%</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>All other PIs</td>
<td>No data</td>
<td></td>
</tr>
<tr>
<td>Contraceptives – Transdermal Ethinyl Estradiol/ Norelgestromin LPV/r</td>
<td></td>
<td>↔ LPV</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ethinyl estradiol AUC ↓ 45%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Norelgestromin AUC ↑ 83%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>All other PIs</td>
<td>No data</td>
<td></td>
</tr>
<tr>
<td>Contraceptives – Vaginal Ring Etonogestrel/Ethinyl Estradiol</td>
<td>ATV/r</td>
<td>Ethinyl estradiol AUC ↓ 26%</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>All other PIs</td>
<td>Etonogestrol AUC ↑ 79%</td>
<td></td>
</tr>
</tbody>
</table>
### Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs  
(Last updated December 18, 2019; last reviewed December 18, 2019)  
(page 15 of 19)

<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 Therapies, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Contraceptives – Vaginal Ring</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Segesterson/Ethinyl Estradiol</td>
<td>All PIs</td>
<td>No data</td>
<td>Use alternative ARV or contraceptive methods.</td>
</tr>
<tr>
<td></td>
<td>PI/c</td>
<td>↓ estradiol possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PI/r</td>
<td>↓ estradiol possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td>All PIs</td>
<td>↔ goserelin, leuprolide acetate, and spironolactone expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>All PIs</td>
<td>↑ dutasteride possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td>All PIs</td>
<td>↑ finasteride possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td>All PIs</td>
<td>↓ testosterone possible</td>
<td></td>
</tr>
<tr>
<td><strong>Gender-Affirming Therapy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>All PIs</td>
<td>↓ or ↑estradiol possible with estradiol or conjugated estrogen (equine and synthetic)</td>
<td>Adjust estradiol dose as needed based on clinical effects and endogenous hormone concentrations.</td>
</tr>
<tr>
<td></td>
<td>All PIs</td>
<td>↑ or ↑ estradiol possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td>All PIs</td>
<td>↑ or ↑ estradiol possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td>All PIs</td>
<td>↑ or ↑estradiol possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td>All PIs</td>
<td>↑ or ↑estradiol possible</td>
<td></td>
</tr>
<tr>
<td><strong>Menopausal Replacement Therapy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>All PIs</td>
<td>↓ or ↑estradiol possible with estradiol or conjugated estrogen (equine and synthetic)</td>
<td>Adjust estradiol dose as needed based on clinical effects.</td>
</tr>
<tr>
<td></td>
<td>All PIs</td>
<td>↑ or ↑estradiol possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td>All PIs</td>
<td>↑ or ↑estradiol possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td>All PIs</td>
<td>↑ or ↑estradiol possible</td>
<td></td>
</tr>
<tr>
<td><strong>Immunosuppressants</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyclosporine, Everolimus, Sirolimus, Tacrolimus</td>
<td>All PIs</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 immunosuppressant-related adverse events. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with specialist as necessary.</td>
</tr>
<tr>
<td><strong>Lipid-Modifying Agents</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>ATV (unboosted), ATV/r</td>
<td>↑ atorvastatin possible</td>
<td>Titrating atorvastatin dose carefully and administer the lowest effective dose while monitoring for toxicities.</td>
</tr>
<tr>
<td></td>
<td>ATV/c</td>
<td>Atorvastatin AUC ↑ 9.2-fold and C&lt;sub&gt;max&lt;/sub&gt; ↑ 18.9-fold</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td>DRV/c</td>
<td>Atorvastatin AUC ↑ 3.9-fold and C&lt;sub&gt;max&lt;/sub&gt; ↑ 4.2-fold</td>
<td>Titrating atorvastatin dose carefully and administer the lowest effective dose while monitoring for toxicities. Do not exceed 20 mg atorvastatin daily.</td>
</tr>
<tr>
<td></td>
<td>DRV/r</td>
<td>DRV/r plus atorvastatin 10 mg similar to atorvastatin 40 mg administered alone</td>
<td>Titrating atorvastatin dose carefully and administer the lowest effective dose while monitoring for toxicities. Do not exceed 20 mg atorvastatin daily.</td>
</tr>
<tr>
<td></td>
<td>LPV/r</td>
<td>Atorvastatin AUC ↑ 5.9-fold and C&lt;sub&gt;max&lt;/sub&gt; ↑ 4.7-fold</td>
<td>Titrating atorvastatin dose carefully and administer the lowest effective dose while monitoring for toxicities. Do not exceed 20 mg atorvastatin daily.</td>
</tr>
<tr>
<td></td>
<td>TPV/r</td>
<td>Atorvastatin AUC ↑ 9.4-fold and C&lt;sub&gt;max&lt;/sub&gt; ↑ 8.6-fold</td>
<td>Do not coadminister.</td>
</tr>
</tbody>
</table>
Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs  *(Last updated December 18, 2019; last reviewed December 18, 2019)*  (page 16 of 19)

<table>
<thead>
<tr>
<th>Concomitant Drug</th>
<th>All PIs except TPV/r</th>
<th>Effect on PI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lomitapide</strong></td>
<td></td>
<td>↑ lomitapide expected</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td></td>
<td>TPV/r</td>
<td>↑ lomitapide expected</td>
<td>Titrate lomitapide dose based on clinical response. Do not exceed lomitapide 30 mg daily.</td>
</tr>
<tr>
<td><strong>Lovastatin</strong></td>
<td>All PIs</td>
<td>Significant ↑ lovastatin expected</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td><strong>Pitavastatin</strong></td>
<td>All PIs</td>
<td>ATV ↑ pitavastatin AUC 31% and C&lt;sub&gt;max&lt;/sub&gt; ↑ 60%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>DRV/r</td>
<td>↓ pitavastatin AUC 26%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LPV/r</td>
<td>↓ pitavastatin AUC 20%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PRV</td>
<td>↑ pitavastatin AUC 23% at steady state</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>No dose adjustment needed.</td>
<td></td>
</tr>
<tr>
<td><strong>Pravastatin</strong></td>
<td>ATV/c, ATV/r</td>
<td>No data</td>
<td>Titrate pravastatin dose carefully while monitoring for pravastatin-related adverse events.</td>
</tr>
<tr>
<td></td>
<td>DRV/c, DRV/r</td>
<td>With DRV/r:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Pravastatin AUC ↑ 81% following single dose of pravastatin</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pravastatin AUC ↑ 23% at steady state</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Titrate pravastatin dose carefully while monitoring for pravastatin-related adverse events.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LPV/r</td>
<td>Pravastatin AUC ↑ 33%</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td><strong>Rosuvastatin</strong></td>
<td>ATV/r</td>
<td>Rosuvastatin AUC ↑ 3-fold and C&lt;sub&gt;max&lt;/sub&gt; ↑ 7-fold</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ATP/c</td>
<td>Rosuvastatin AUC ↑ 3.4-fold and 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 and C&lt;sub&gt;max&lt;/sub&gt; ↑ 3.8-fold</td>
<td></td>
</tr>
<tr>
<td></td>
<td>DRV/r</td>
<td>Rosuvastatin AUC ↑ 48% and C&lt;sub&gt;max&lt;/sub&gt; ↑ 2.4-fold</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LPV/r</td>
<td>Rosuvastatin AUC ↑ 2.1-fold and C&lt;sub&gt;max&lt;/sub&gt; ↑ 4.7-fold</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TPV/r</td>
<td>Rosuvastatin AUC ↑ 26% and C&lt;sub&gt;max&lt;/sub&gt; ↑ 2.2-fold</td>
<td></td>
</tr>
<tr>
<td><strong>Simvastatin</strong></td>
<td>All PIs</td>
<td>Significant ↑ simvastatin expected</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td><strong>Narcotics and Treatment for Opioid Dependence</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Buprenorphine</strong></td>
<td>Sublingual, buccal, or implant</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ATV (unboosted)</td>
<td>Buprenorphine AUC ↑ 93% Norbuprenorphine (active metabolite) AUC ↑ 76%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ ATV possible</td>
<td>Do not coadminister.</td>
</tr>
</tbody>
</table>
### Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs  (Last updated December 18, 2019; last reviewed December 18, 2019)  (page 17 of 19)

<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>Narcotics and Treatment for Opioid Dependence, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Buprenorphine</strong> Sublingual, buccal, or implant, continued</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ATV/r</td>
<td>Buprenorphine AUC ↑ 66% Norbuprenorphine (active metabolite) AUC ↑ 105%</td>
<td>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.</td>
</tr>
<tr>
<td></td>
<td>DRV/r</td>
<td>↔ buprenorphine Norbuprenorphine (active metabolite) AUC ↑ 46% and C&lt;sub&gt;min&lt;/sub&gt; ↑ 71%</td>
<td>No dose adjustment needed. Monitor for buprenorphine-related adverse events. When transferring buprenorphine from transmucosal delivery to implantation, monitor to ensure buprenorphine effect is adequate and not excessive.</td>
</tr>
<tr>
<td></td>
<td>LPV/r</td>
<td>↔ LPV/r</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TPV/r</td>
<td>↔ buprenorphine Norbuprenorphine (active metabolite) AUC, C&lt;sub&gt;max&lt;/sub&gt; and C&lt;sub&gt;min&lt;/sub&gt; ↓ 80% TPV C&lt;sub&gt;min&lt;/sub&gt; ↓ 19% to 40%</td>
<td>Consider monitoring TPV concentration. When transferring buprenorphine from transmucosal delivery to implantation, monitor to ensure buprenorphine effect is adequate and not excessive.</td>
</tr>
<tr>
<td></td>
<td>PI/c</td>
<td>No data</td>
<td>Monitor for buprenorphine-related adverse events.</td>
</tr>
<tr>
<td><strong>Fentanyl</strong></td>
<td>All PIs</td>
<td>↑ fentanyl possible</td>
<td>Monitor for fentanyl-related adverse events, including potentially fatal respiratory depression.</td>
</tr>
<tr>
<td><strong>Lofexidine</strong></td>
<td>ATP (unboosted)</td>
<td>↔ lofexidine expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>PI/c, PI/r</td>
<td>↑ lofexidine possible</td>
<td>Monitor for lofexidine-related adverse events, including symptoms of orthostasis and bradycardia.</td>
</tr>
<tr>
<td><strong>Methadone</strong></td>
<td>ATP (unboosted)</td>
<td>↔ ATP</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>PI/c</td>
<td>No data</td>
<td>Titrate methadone dose using the lowest feasible initial dose. Dose adjustment of methadone may be needed. Monitor for methadone-related adverse events.</td>
</tr>
<tr>
<td></td>
<td>All PI/r</td>
<td>ATP/r and DRV/r ↓ R-methadone&lt;sup&gt;d&lt;/sup&gt; AUC 16% to 18% LPV/r ↓ methadone AUC 26% to 53% TPV/r ↓ R-methadone&lt;sup&gt;d&lt;/sup&gt; AUC 48%</td>
<td>Opioid withdrawal is unlikely but may occur. Monitor for opioid withdrawal and increase methadone dose as clinically indicated.</td>
</tr>
<tr>
<td><strong>Oxycodone</strong></td>
<td>All PIs</td>
<td>LPV/r ↑ oxycodone AUC 2.6-fold Other PIs: ↑ oxycodone expected</td>
<td>Monitor for opioid-related adverse events. Oxycodone dose reduction may be necessary.</td>
</tr>
<tr>
<td><strong>Tramadol</strong></td>
<td>All PIs</td>
<td>↑ tramadol expected ↓ M1 (active metabolite) possible</td>
<td>Tramadol dose adjustments may be necessary. Monitor for clinical response and tramadol-related adverse events.</td>
</tr>
<tr>
<td><strong>PDE5 Inhibitors</strong></td>
<td>Avanafil</td>
<td>ATP (unboosted)</td>
<td>No data</td>
</tr>
<tr>
<td></td>
<td>PI/c, PI/r</td>
<td>RTV 600 mg twice daily (for 5 days) ↑ avanafil AUC 13-fold and ↑ C&lt;sub&gt;max&lt;/sub&gt; 2.4-fold</td>
<td>Do not coadminister.</td>
</tr>
</tbody>
</table>
### Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs  *(Last updated December 18, 2019; last reviewed December 18, 2019)*  

<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>PDE5 Inhibitors, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sildenafil</td>
<td>All PIs</td>
<td>DRV/r plus sildenafil 25 mg similar to sildenafil 100 mg alone&lt;br&gt;RTV 500 mg twice daily ↑ sildenafil AUC 1,000%&lt;br&gt;RTV 200 mg twice daily ↑ sildenafil AUC 124%&lt;br&gt;TPV/r (first dose) ↑ tadalafil AUC 133%</td>
<td><em>For Treatment of Erectile Dysfunction:</em>&lt;br&gt;Start with sildenafil 25 mg every 48 hours and monitor for adverse events of sildenafil.&lt;br&gt;<em>Contraindicated</em> for treatment of PAH.</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&lt;br&gt;RTV 200 mg twice daily (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><em>Oral midazolam is contraindicated with PIs.</em>&lt;br&gt;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><em>Do not coadminister.</em></td>
</tr>
<tr>
<td>Triazolam</td>
<td>All PIs</td>
<td>↑ triazolam expected&lt;br&gt;RTV 200 mg twice daily ↑ triazolam half-life 1,200% and ↑ AUC 2,000%</td>
<td><em>Contraindicated.</em></td>
</tr>
<tr>
<td>Zolpidem</td>
<td>PI/c, PI/r</td>
<td>↑ zolpidem possible</td>
<td>Initiate zolpidem at a low dose. Dose reduction may be necessary.</td>
</tr>
</tbody>
</table>
Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 19 of 19)

<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</strong></td>
<td></td>
<td></td>
<td></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>
<tr>
<td>Colchicine</td>
<td>All PIs</td>
<td>RTV 100 mg twice daily ↑ colchicine AUC 296% and C&lt;sub&gt;max&lt;/sub&gt; ↑ 184% Significant ↑ colchicine expected with all PIs, with or without COBI or RTV</td>
<td>For Treatment of Gout Flares: • Administer a single dose of colchicine 0.6 mg, followed by colchicine 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 twice daily, decrease to colchicine 0.3 mg once daily. If dose 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 colchicine 0.3 mg twice daily. Do not coadminister in patients with hepatic or renal impairment.</td>
</tr>
<tr>
<td>Dronabinol</td>
<td>All PIs</td>
<td>↑ dronabinol possible</td>
<td>Monitor for dronabinol-related adverse events.</td>
</tr>
<tr>
<td>Eluxadoline</td>
<td>All PIs</td>
<td>↑ eluxadoline expected</td>
<td>Administer eluxadoline at a dose of 75 mg twice daily and monitor for eluxadoline-related adverse events.</td>
</tr>
<tr>
<td>Ergot Derivatives</td>
<td>All PIs</td>
<td>↑ dihydroergotamine, ergotamine, and methylergonovine expected</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td>Fibanserin</td>
<td>All PIs</td>
<td>↑ fibanserin expected</td>
<td>Contraindicated.</td>
</tr>
</tbody>
</table>

* DHA is an active metabolite of artemether.

b The following products contain no more than 30 mcg of ethinyl estradiol combined with norethindrone or norgestimate: 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. Generic formulations may also be available.

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

d R-methadone is the active form of methadone.

Key to Symbols:
† = increase
↓ = decrease
↔ = no change

Key: 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; CCB = calcium channel blocker; C<sub>max</sub> = maximum plasma concentration; C<sub>min</sub> = minimum plasma concentration; CNS = central nervous system; COBI = 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; FDA = Food and Drug Administration; FPV = fosamprenavir; H2RA = H2 receptor antagonist; HCV = hepatitis C virus; HRT = hormone replacement therapy; IDV = indinavir; INR = international normalized ratio; LPV = lopinavir; LPV/r = lopinavir/ritonavir; MPA = medroxyprogesterone acetate; NFV = nelfinavir; OATP = organic anion-transporting polypeptide; PAH = pulmonary arterial hypertension; PDE5 = phosphodiesterase Type 5; 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 = ritonavir; SQV = saquinavir; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant; TDF = tenofovir disoproxil fumarate; TPV = tipranavir; TPV/r = tipranavir/ritonavir; VPA = valproic acid

Downloaded from https://aidsinfo.nih.gov/guidelines on 7/3/2020
Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 1 of 12)

This table provides information on the known or predicted interactions between NNRTIs and non-ARV drugs. For information regarding interactions between NNRTIs and other ARV drugs, including dosing recommendations, refer to Tables 21c, 22a, and 22b. 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. In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgement to select the most appropriate alternative medication to use.

Note: DLV is not included in this table. Please refer to the FDA product label for information regarding drug interactions between DLV and other concomitant drugs. The term “All NNRTIs” in this table refers to all NNRTIs except for DLV.

<table>
<thead>
<tr>
<th>Concomitant Drug</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>Acid Reducers</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antacids</td>
<td>DOR, EFV, NVP</td>
<td>↔ NNRTI AUC</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>↔ ETR expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></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>DOR, ETR, NVP</td>
<td>↔ NNRTI expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV</td>
<td>↔ EFV AUC</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>RPV AUC ↓ 76% when famotidine 40 mg is taken 2 hours prior</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>DOR</td>
<td>DOR AUC ↓ 17% and C_{min} ↓ 16%</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV, NVP</td>
<td>↔ EFV and NVP expected</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>↔ ETR AUC</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>With Omeprazole 20 mg Daily: • RPV AUC ↓ 40% and C_{min} ↓ 33%</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td><strong>Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alfuzosin, Doxazosin, Silodosin</td>
<td>DOR, RPV</td>
<td>↔ alpha-adrenergic antagonists expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↓ alpha-adrenergic antagonists expected</td>
<td>Consider alternative ARV or alpha antagonist therapy. If coadministration is necessary, monitor for therapeutic effectiveness of alpha antagonist.</td>
</tr>
<tr>
<td>Tamsulosin</td>
<td>DOR, RPV</td>
<td>↔ tamsulosin expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↓ tamsulosin expected</td>
<td>Monitor for therapeutic effectiveness of tamsulosin after 2–4 weeks. May need to increase dose to tamsulosin 0.8 mg once daily for patients who fail to respond to the 0.4 mg dose.</td>
</tr>
<tr>
<td><strong>Antibacterials</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bedaquiline</td>
<td>DOR, RPV</td>
<td>↔ bedaquiline expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></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 needed.</td>
</tr>
<tr>
<td>Concomitant Drug</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>Antibacterials, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rifabutin</td>
<td>DOR</td>
<td>DOR AUC ↓ 50%</td>
<td>Increase DOR dose to 100 mg twice daily. No dose adjustment needed for rifabutin.</td>
</tr>
<tr>
<td></td>
<td>EFV</td>
<td>Rifabutin ↓ 38%</td>
<td>The recommended dosing range is rifabutin 450–600 mg per day.</td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>↔ rifabutin and metabolite AUC</td>
<td>Do not coadminister ETR plus PI/r with rifabutin.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ETR AUC ↓ 37%</td>
<td>Use rifabutin 300 mg once daily if ETR is administered without PI/r.</td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>Rifabutin AUC ↑ 17% and metabolite AUC ↑ 24%</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NVP C_{min} ↓ 16%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>Rifabutin plus RPV 50 mg Once Daily Compared to RPV 25 mg Once Daily Alone:</td>
<td>Increase RPV dose to 50 mg once daily. No dose adjustment for rifabutin needed.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↔ RPV AUC and C_{min}</td>
<td></td>
</tr>
<tr>
<td><strong>Rifampin</strong></td>
<td>DOR</td>
<td>DOR AUC ↓ 88%</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td></td>
<td>EFV</td>
<td>EFV AUC ↓ 26%</td>
<td>Do not use EFV 400 mg with rifampin. Maintain EFV dose at 600 mg once daily and monitor for virologic response.</td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>Significant ↓ ETR possible</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>NVP ↓ 20% to 58%</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>RPV AUC ↓ 80%</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td><strong>Rifapentine</strong></td>
<td>DOR, RPV</td>
<td>↓ NNRTI expected</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td></td>
<td>EFV</td>
<td>↔ EFV concentrations</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>ETR, NVP</td>
<td>↓ NNRTI possible</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td><strong>Macrolides</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azithromycin</td>
<td>All NNRTIs</td>
<td>↔ azithromycin expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>DOR, RPV</td>
<td>↔ clarithromycin expected</td>
<td>Consider alternative macrolide (e.g., azithromycin) for MAC prophylaxis and treatment.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ DOR and RPV possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td>EFV</td>
<td>Clarithromycin AUC ↓ 39%</td>
<td>Monitor for effectiveness or consider alternative agent (e.g., azithromycin) for MAC prophylaxis and treatment.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ETR AUC ↑ 42%</td>
<td>Consider alternative macrolide (e.g., azithromycin) for MAC prophylaxis and treatment.</td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>Clarithromycin AUC ↓ 31%</td>
<td>Monitor for effectiveness or consider alternative macrolide (e.g., azithromycin) for MAC prophylaxis and treatment.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NVP AUC ↑ 26%</td>
<td></td>
</tr>
<tr>
<td>Erythromycin</td>
<td>DOR, RPV</td>
<td>↑ DOR and RPV possible</td>
<td>Monitor for ARV tolerability if used in combination.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↑ EFV, ETR, and NVP possible</td>
<td>Monitor for antibiotic efficacy if used in combination.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ erythromycin possible</td>
<td></td>
</tr>
<tr>
<td><strong>Anticoagulants</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apixaban</td>
<td>DOR, RPV</td>
<td>↔ apixaban expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↓ apixaban possible</td>
<td>Consider alternative ARV or anticoagulant therapy.</td>
</tr>
</tbody>
</table>
Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs  *(Last updated December 18, 2019; last reviewed December 18, 2019)*  (page 3 of 12)

<table>
<thead>
<tr>
<th>Concomitant Drug</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>Anticoagulants, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Betrixaban</td>
<td>All NNRTIs</td>
<td>↔ betrixaban expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>Dabigatran</td>
<td>All NNRTIs</td>
<td>↔ dabigatran expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>All NNRTIs</td>
<td>↔ edoxaban expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td><strong>Rivaroxaban</strong></td>
<td>DOR, RPV</td>
<td>↔ rivaroxaban expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↓ rivaroxaban possible</td>
<td>Consider alternative ARV or anticoagulant therapy.</td>
</tr>
<tr>
<td><strong>Warfarin</strong></td>
<td>DOR, RPV</td>
<td>↔ warfarin expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</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, Phenobarbital, Phenytoin</td>
<td>DOR, RPV</td>
<td>↓ NNRTI possible</td>
<td><strong>Contraindicated.</strong></td>
</tr>
<tr>
<td>EFV</td>
<td></td>
<td>Carbamazepine plus EFV:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Carbamazepine AUC ↓ 27%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• EFV AUC ↓ 36%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phenytoin plus EFV:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• ↓ EFV</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• ↑ or ↓ phenytoin possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>↓ anticonvulsant and ETR possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>↓ anticonvulsant and NVP possible</td>
<td><strong>Contraindicated.</strong></td>
</tr>
<tr>
<td><strong>Eslicarbazepine</strong></td>
<td>All NNRTIs</td>
<td>↓ NNRTI possible</td>
<td>Consider alternative ARV or anticonvulsant and NVP concentrations and virologic response.</td>
</tr>
<tr>
<td><strong>Oxcarbazepine</strong></td>
<td>DOR, RPV</td>
<td>↔ anticonvulsant expected</td>
<td><strong>Contraindicated.</strong></td>
</tr>
<tr>
<td>EFV, ETR, NVP</td>
<td>↓ anticonvulsant possible</td>
<td>Consider alternative ARV or anticonvulsant. If coadministration is necessary, monitor anticonvulsant and NVP concentrations.</td>
<td></td>
</tr>
<tr>
<td>Ethosuximide, Lacosamide, Tiagabine, Zonisamide</td>
<td>DOR, RPV</td>
<td>↔ lamotrigine expected</td>
<td><strong>No dose adjustment needed.</strong></td>
</tr>
<tr>
<td>EFV, ETR, NVP</td>
<td>↓ anticonvulsant possible</td>
<td>Monitor seizure control and plasma concentrations of lamotrigine.</td>
<td></td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>DOR, ETR, RPV</td>
<td>↔ lamotrigine expected</td>
<td><strong>No dose adjustment needed.</strong></td>
</tr>
<tr>
<td>EFV</td>
<td>↓ lamotrigine possible</td>
<td>Monitor seizure control and plasma concentrations of lamotrigine.</td>
<td></td>
</tr>
<tr>
<td>NVP</td>
<td>↓ lamotrigine possible</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Antidepressants, Anxiolytics, and Antipsychotics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Antidepressants</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bupropion</td>
<td>DOR, ETR, RPV</td>
<td>↔ bupropion expected</td>
<td><strong>No dose adjustment needed.</strong></td>
</tr>
<tr>
<td>EFV</td>
<td>Bupropion AUC ↓ 55%</td>
<td>Titrate bupropion dose based on clinical response.</td>
<td></td>
</tr>
<tr>
<td>NVP</td>
<td>↓ bupropion possible</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs  (Last updated December 18, 2019; last reviewed December 18, 2019) (page 4 of 12)

<table>
<thead>
<tr>
<th>Concomitant Drug</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>Antidepressants, Anxiolytics, and Antipsychotics, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Antidepressants, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citalopram, Escitalopram</td>
<td>DOR, RPV</td>
<td>↔ antidepressant expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↓ antidepressant possible</td>
<td>Titrated antidepressant dose based on clinical response.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluoxetine, Fluvoxamine</td>
<td>All NNRTIs</td>
<td>↔ antidepressant expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paroxetine</td>
<td>DOR, NVP, RPV</td>
<td>↔ paroxetine expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR</td>
<td>↔ paroxetine expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>Nefazodone</td>
<td>DOR, RPV</td>
<td>↑ NNRTI possible</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↓ nefazodone expected</td>
<td>Monitor antidepressant effect and titrate dose as necessary based on clinical response.</td>
</tr>
<tr>
<td>Sertraline</td>
<td>DOR, RPV</td>
<td>↔ sertraline expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV</td>
<td>Sertraline AUC ↓ 39%</td>
<td>Monitor the antidepressant effect and titrate dose as necessary based on clinical response.</td>
</tr>
<tr>
<td></td>
<td>ETR, NVP</td>
<td>↓ sertraline possible</td>
<td></td>
</tr>
<tr>
<td>Trazodone</td>
<td>DOR, RPV</td>
<td>↔ trazodone expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↓ trazodone possible</td>
<td>Monitor for therapeutic effectiveness of trazodone and titrate dose as necessary.</td>
</tr>
<tr>
<td>Alprazolam, Triazolam</td>
<td>DOR, RPV</td>
<td>↔ benzodiazepine expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↓ benzodiazepine possible</td>
<td>Monitor for therapeutic effectiveness of benzodiazepine.</td>
</tr>
<tr>
<td>Diazepam</td>
<td>DOR, RPV</td>
<td>↔ diazepam expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV, NVP</td>
<td>↓ diazepam possible</td>
<td>Monitor for therapeutic effectiveness of diazepam.</td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>↑ diazepam possible</td>
<td>Decreased dose of diazepam may be necessary. Monitor for diazepam toxicity.</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>DOR, ETR, NVP, RPV</td>
<td>↔ lorazepam expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV</td>
<td>↔ lorazepam AUC</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>Midazolam</td>
<td>DOR, RPV</td>
<td>↔ midazolam expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV</td>
<td>↑ or ↓ midazolam possible</td>
<td>Monitor for therapeutic effectiveness and toxicity of midazolam.</td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>Midazolam AUC ↓ 31%</td>
<td>Midazolam active metabolite $C_{\text{max}}$ ↑ 57%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Monitor for therapeutic effectiveness of midazolam.</td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>↓ midazolam possible</td>
<td>Monitor for therapeutic effectiveness of midazolam.</td>
</tr>
<tr>
<td><strong>Antipsychotics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>DOR, RPV</td>
<td>↔ aripiprazole expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↓ aripiprazole expected</td>
<td>Monitor for therapeutic effectiveness of antipsychotic. Consider doubling usual dose of aripiprazole over 1–2 weeks. Refer to aripiprazole prescribing information for dose recommendations.</td>
</tr>
</tbody>
</table>
### Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 5 of 12)

<table>
<thead>
<tr>
<th>Concomitant Drug</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>Antipsychotics, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brexpiprazole</td>
<td>DOR, RPV</td>
<td>↔ brexpiprazole expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↓ brexpiprazole expected</td>
<td>Monitor for therapeutic effectiveness of antipsychotic. Consider doubling the usual dose of brexpiprazole and making further adjustments based on clinical response. Refer to brexpiprazole prescribing information.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↓ cariprazine and ↑ or ↓ active metabolite possible</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td>Cariprazine</td>
<td>DOR, RPV</td>
<td>↔ antipsychotic expected</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↓ antipsychotic possible</td>
<td>Monitor for therapeutic effectiveness of antipsychotic.</td>
</tr>
<tr>
<td></td>
<td>Lurasidone</td>
<td>DOR, RPV</td>
<td>↔ lurasidone expected</td>
</tr>
<tr>
<td></td>
<td>EFV</td>
<td>↓ lurasidone possible</td>
<td>Monitor for therapeutic effectiveness of lurasidone.</td>
</tr>
<tr>
<td></td>
<td>Pimavanserin</td>
<td>DOR, RPV</td>
<td>↔ pimavanserin expected</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↓ pimavanserin expected</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td>Olanzapine</td>
<td>DOR, ETR, NVP, RPV</td>
<td>↔ olanzapine expected</td>
</tr>
<tr>
<td></td>
<td>EFV</td>
<td>↓ olanzapine possible</td>
<td>Monitor for therapeutic effectiveness of olanzapine.</td>
</tr>
<tr>
<td></td>
<td>Pimozide</td>
<td>DOR, RPV</td>
<td>↔ pimozide expected</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↓ pimozide possible</td>
<td>Monitor for therapeutic effectiveness of pimozide.</td>
</tr>
<tr>
<td></td>
<td>Quetiapine</td>
<td>DOR, RPV</td>
<td>↔ antipsychotic expected</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↓ antipsychotic possible</td>
<td>Monitor for therapeutic effectiveness of antipsychotic.</td>
</tr>
<tr>
<td><strong>Antifungals</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluconazole</td>
<td>DOR, RPV</td>
<td>↑ NNRTI possible</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV</td>
<td>↔ fluconazole expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↔ EFV AUC expected</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>ETR AUC ↑ 86%</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>NVP AUC ↑ 110%</td>
<td>Consider alternative ARV or antifungal agent. Increased risk of hepatotoxicity possible with this combination.</td>
</tr>
<tr>
<td>Isavuconazole</td>
<td>DOR, RPV</td>
<td>↑ NNRTI possible</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↓ isavuconazole possible</td>
<td>Monitor isavuconazole concentration and antifungal response. Dose adjustments for isavuconazole may be necessary.</td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>↓ itraconazole possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ ETR possible</td>
<td>Dose adjustments for itraconazole may be necessary. Monitor itraconazole concentration and antifungal response.</td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>Itraconazole AUC ↓ 61%</td>
<td>Do not coadminister, unless potential benefits outweigh the risks. If coadministration is necessary, monitor itraconazole concentration and adjust dose accordingly.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ NVP possible</td>
<td></td>
</tr>
</tbody>
</table>
### Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs  *(Last updated December 18, 2019; last reviewed December 18, 2019)*

<table>
<thead>
<tr>
<th>Concomitant Drug</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>Antifungals, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posaconazole</td>
<td>DOR, ETR, NVP, RPV</td>
<td>↑ NNRTI possible</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV</td>
<td>Posaconazole AUC ↓ 50% → EFV AUC</td>
<td><strong>Do not coadminister, unless potential benefits outweigh the risks.</strong> If coadministration is necessary, monitor posaconazole concentration and adjust dose accordingly.</td>
</tr>
<tr>
<td>Voriconazole</td>
<td>DOR, RPV</td>
<td>↑ NNRTI possible</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV</td>
<td>Voriconazole AUC ↓ 77% EFV AUC ↑ 44%</td>
<td><strong>Contraindicated at standard doses.</strong> Adjust dose to voriconazole 400 mg twice daily plus EFV 300 mg daily.</td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>↔ voriconazole AUC ETR AUC ↑ 36%</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>↓ voriconazole possible ↑ NVP possible</td>
<td>Consider alternative ARV or antifungal agent. If coadministration is necessary, monitor antiretroviral tolerability and antifungal response and/or voriconazole concentration.</td>
</tr>
<tr>
<td><strong>Antimalarials</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Artemether/ Lumefantrine</td>
<td>DOR, RPV</td>
<td>↔ antimalarial expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV</td>
<td>Artemether AUC ↓ 79% DHA AUC ↓ 75% Lumefantrine AUC ↓ 56%</td>
<td>Consider alternative ARV or antimalarial drug. If used in combination, monitor closely for antimalarial efficacy.</td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>Artemether AUC ↓ 38% ↔ DHA AUC ↔ lumefantrine AUC ↔ ETR AUC</td>
<td>Clinical significance of the reduced antimalarial drug concentrations unknown. If used in combination with ETR, monitor for antimalarial efficacy.</td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>Artemether AUC ↓ 67% to 72% DHA: Study results are conflicting. DHA AUC ↓ 37% in one study, no difference in another. Lumefantrine: Study results are conflicting. Lumefantrine AUC ↓ 25% to 58% in two studies but ↑ 56% in another.</td>
<td>Clinical significance unknown. If used in combination, monitor closely for antimalarial efficacy and lumefantrine toxicity.</td>
</tr>
<tr>
<td>Atovaquone/ Proguanil</td>
<td>DOR, ETR, NVP, RPV</td>
<td>No data</td>
<td>Monitor for antimalarial efficacy.</td>
</tr>
<tr>
<td></td>
<td>EFV</td>
<td>Atovaquone AUC ↓ 75% Proguanil AUC ↓ 43%</td>
<td>No dose recommendation. Consider alternative drug for malaria prophylaxis, if possible.</td>
</tr>
</tbody>
</table>
Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs  *(Last updated December 18, 2019; last reviewed December 18, 2019)* (page 7 of 12)

<table>
<thead>
<tr>
<th>Concomitant Drug</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>Antiplatelets</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>DOR, NVP, RPV</td>
<td>↔ clopidogrel expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR</td>
<td>↓ activation of clopidogrel possible</td>
<td>Consider alternative ARV or antiplatelet. ETR may prevent metabolism of clopidogrel to its active metabolite.</td>
</tr>
<tr>
<td>Prasugrel</td>
<td>All NNRTIs</td>
<td>↔ prasugrel expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>Ticagrelor</td>
<td>DOR, RPV</td>
<td>↔ ticagrelor expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↓ ticagrelor expected</td>
<td>Consider alternative ARV or anticoagulant therapy.</td>
</tr>
<tr>
<td>Vorapaxar</td>
<td>DOR, NVP, RPV</td>
<td>↔ vorapaxar expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR</td>
<td>↓ vorapaxar expected</td>
<td>Insufficient data to make a dose recommendation.</td>
</tr>
</tbody>
</table>

**Antipneumocystis and Anti-Toxoplasmosis Drugs**

<table>
<thead>
<tr>
<th>Drug</th>
<th>NNRTI</th>
<th>Effect on ATG and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atovaquone (oral solution)</td>
<td>DOR, ETR, RPV, NVP</td>
<td>No data</td>
<td>Monitor for therapeutic effectiveness of atovaquone.</td>
</tr>
<tr>
<td></td>
<td>EFV</td>
<td>Atovaquone AUC ↓ 44% to 47%</td>
<td></td>
</tr>
<tr>
<td><strong>Cardiac Medications</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dihydropyridine CCBs</td>
<td>DOR, RPV</td>
<td>↔ CCBs expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↓ CCBs possible</td>
<td>Titrates CCB dose based on clinical response.</td>
</tr>
<tr>
<td>Diltiazem, Verapamil</td>
<td>DOR, RPV</td>
<td>↔ NNRTI possible</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV</td>
<td>Diltiazem AUC ↓ 69%</td>
<td>Titrates diltiazem or verapamil dose based on clinical response.</td>
</tr>
<tr>
<td></td>
<td>ETR, NVP</td>
<td>↓ diltiazem or verapamil possible</td>
<td></td>
</tr>
<tr>
<td><strong>Corticosteroids</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>DOR, ETR, RPV</td>
<td>↓ NNRTI possible</td>
<td>Consider alternative corticosteroid for long-term use. If dexamethasone is used with NNRTI, monitor virologic response.</td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>Significant ↓ RPV possible</td>
<td>Contraindicated with more than a single dose of dexamethasone.</td>
</tr>
<tr>
<td><strong>Glucose-Lowering Agents</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canagliflozin, Dapagliflozin, Empagliflozin, Sitagliptin</td>
<td>All NNRTIs</td>
<td>↔ antihyperglycemic expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>Linagliptin, Saxagliptin</td>
<td>DOR, RPV</td>
<td>↔ antihyperglycemic expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↓ antihyperglycemic possible</td>
<td>Monitor glycemic control.</td>
</tr>
<tr>
<td>Metformin</td>
<td>DOR</td>
<td>↔ metformin AUC</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP, RPV</td>
<td>↓ metformin expected</td>
<td></td>
</tr>
<tr>
<td>Concomitant Drug</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>Hepatitis C Direct-Acting Antiviral Agents</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daclatasvir</td>
<td>DOR, RPV</td>
<td>No data</td>
<td>No dose adjustment needed.</td>
</tr>
</tbody>
</table>
|                  | EFV, ETR, NVP | Daclatasvir 120 mg Once Daily plus EFV 600 mg Daily Compared with Daclatasvir 60 mg Alone:  
• Daclatasvir C_{min} ↓ 17% and AUC ↑ 37% | The recommended dose is daclatasvir 90 mg once daily. |
|                  | ETR, NVP | ↓ DAAs possible | Do not coadminister. |
|                  | RPV | RPV AUC ↑ 150% to 225% | Do not coadminister, due to potential for QT interval prolongation with higher concentrations of RPV. |
| Elbasvir/ Grazoprevir | DOR | ↑ DOR possible | No dose adjustment needed. |
|                  | EFV | No data | Contraindicated. |
|                  | ETR, NVP | ↓ elbasvir and grazoprevir expected | Do not coadminister. |
|                  | RPV | ↔ elbasvir and grazoprevir  
↔ RPV AUC and C_{min} | No dose adjustment needed. |
|                  | NVP | ↓ glecaprevir and pibrentasvir possible | Consider alternative ARV or HCV regimen. If coadministration is necessary, monitor for HCV treatment efficacy. |
|                  | | | |
| Glecaprevir/ Pibrentasvir | DOR | ↑ DOR expected | No dose adjustment needed. |
|                  | EFV | ↓ glecaprevir and pibrentasvir expected | Do not coadminister. |
|                  | ETR | ↓ glecaprevir and pibrentasvir possible | |
|                  | RPV | ↔ glecaprevir and pibrentasvir  
RPV AUC ↑ 84% | No dose adjustment needed. |
| Sofosbuvir/ Ledipasvir | DOR, RPV | No significant effect expected | No dose adjustment needed. |
|                  | EFV | Velpatasvir AUC ↓ 43%, C_{max} ↓ 37%, and C_{min} ↓ 47% | Do not coadminister. |
|                  | ETR, NVP | ↓ velpatasvir expected | Do not coadminister. |
| Sofosbuvir/ Velpatasvir/ Voxilaprevir | DOR, RPV | No significant effect expected | No dose adjustment needed. |
|                  | EFV | Velpatasvir AUC ↓ 43%, C_{max} ↓ 37%, and C_{min} ↓ 47%  
↓ voxilaprevir expected | Do not coadminister. |
|                  | ETR, NVP | ↓ voxilaprevir expected  
↓ velpatasvir expected | Do not coadminister. |
<table>
<thead>
<tr>
<th>Concomitant Drug</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>Herbal Products</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>St. John’s Wort</td>
<td>DOR, RPV</td>
<td>↓ NNRTI expected</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↓ EFV, ETR, and NVP expected</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td>Hormonal Therapies</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contraceptives –Injectable Depot MPA</td>
<td>DOR, ETR, RPV</td>
<td>↔ MPA expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV, NVP</td>
<td>↔ MPA</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>Contraceptives – Oral</td>
<td>DOR</td>
<td>↔ ethinyl estradiol</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↔ levonorgestrel</td>
<td></td>
</tr>
<tr>
<td></td>
<td>EFV</td>
<td>↔ ethinyl estradiol</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Etonogestrel (metabolite of oral desogestrel) C&lt;sub&gt;min&lt;/sub&gt; ↓ 61%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Levonorgestrel (metabolite of oral norgestimate) AUC ↓ 83%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Norelgestromin (metabolite of oral norgestimate) AUC ↓ 64%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>Ethinyl estradiol AUC ↑ 22%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>↔ norethindrone</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>Ethinyl estradiol AUC ↓ 29% and C&lt;sub&gt;min&lt;/sub&gt; ↓ 58%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Norethindrone AUC ↓ 18%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Etonogestrel (metabolite of oral desogestrel) C&lt;sub&gt;min&lt;/sub&gt; ↓ 22%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>↔ ethinyl estradiol</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↔ norethindrone</td>
<td></td>
</tr>
<tr>
<td>Contraceptives –Subdermal Implant Etonogestrel</td>
<td>DOR, RPV</td>
<td>↔ etonogestrel expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV</td>
<td>Etonogestrel AUC ↓ 63% to 82%</td>
<td>Use alternative ARV or contraceptive methods.</td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>↓ etonogestrel possible</td>
<td>No data available to make dose recommendation.</td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>↔ etonogestrel</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>Contraceptives –Subdermal Implant Levonorestrel</td>
<td>DOR, RPV</td>
<td>↔ levonorgestrel expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV</td>
<td>Levonorgestrel AUC ↓ 47%</td>
<td>Use alternative ARV or contraceptive methods.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unintended pregnancies were observed in women who used EFV and levonorgestrel implant concomitantly.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>↓ levonorgestrel possible</td>
<td>No data available to make dose recommendation.</td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>Levonorgestrel AUC ↑ 35%</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>Contraceptives – Vaginal Ring Etonogestrel/ Ethinyl Estradiol</td>
<td>DOR, RPV</td>
<td>↔ etonogestrel and ethinyl estradiol expected</td>
<td>No dose adjustment needed.</td>
</tr>
</tbody>
</table>

_Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 9 of 12)_

*Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV*
### Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 10 of 12)

<table>
<thead>
<tr>
<th>Concomitant Drug</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>Contraceptives – Vaginal Ring</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Etonogestrel/ Ethinyl Estradiol</td>
<td>EFV</td>
<td>Ethinyl estradiol (intravaginal ring) AUC ↓ 56%</td>
<td>Consider alternative ARV or contraceptive method.</td>
</tr>
<tr>
<td></td>
<td>ETR, NVP</td>
<td>↓ etonogestrel and ethinyl estradiol possible</td>
<td>No data available to make dose recommendation.</td>
</tr>
<tr>
<td></td>
<td>DOR, RPV</td>
<td>↔ segesterone and ethinyl estradiol expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↓ segesterone and ethinyl estradiol possible</td>
<td>Consider alternative ARV or contraceptive method.</td>
</tr>
<tr>
<td>Segesterone/ Ethinyl Estradiol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emergency Contraceptives</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levonorgestrel (oral)</td>
<td>DOR, RPV</td>
<td>↔ levonorgestrel expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV</td>
<td>Levonorgestrel AUC ↓ 58%</td>
<td>Effectiveness of emergency postcoital contraception may be diminished.</td>
</tr>
<tr>
<td></td>
<td>NVP, ETR</td>
<td>↓ levonorgestrel possible</td>
<td>No data available to make dose recommendation.</td>
</tr>
<tr>
<td>Gender-Affirming Therapy</td>
<td>DOR, RPV</td>
<td>↔ hormonal concentrations expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↓ estradiol possible</td>
<td>Monitor feminizing effects of estrogen and antiandrogen therapy and titrate dose as necessary to achieve therapeutic goals.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↔ goserelin, leuprolide acetate, and spironolactone expected</td>
<td></td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↓ dutasteride and finasteride possible</td>
<td></td>
</tr>
<tr>
<td>Menopausal Replacement Therapy</td>
<td>DOR, RPV</td>
<td>↔ hormonal concentrations expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↓ estrogen possible with estradiol or conjugated estrogen (equine and synthetic)</td>
<td>Monitor menopausal symptoms. Titrate to the dose of hormonal therapy that achieves menopausal symptom relief.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↓ medroxyprogesterone possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↓ micronized progesterone possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>↓ drospirenone possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>See Contraceptives – Oral for other progestin-NNRTI interactions</td>
<td></td>
</tr>
<tr>
<td>Immunosuppressants</td>
<td>DOR, RPV</td>
<td>↔ immunosuppressant expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></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></td>
<td>EFV, ETR, NVP</td>
<td>↑ NNRTI possible</td>
<td></td>
</tr>
</tbody>
</table>
### Lipid-Modifying Agents

<table>
<thead>
<tr>
<th>Concomitant Drug</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>Atorvastatin</strong></td>
<td>DOR, RPV, NVP</td>
<td>↔ atorvastatin AUC</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR</td>
<td>Atorvastatin AUC ↓ 32% to 43%</td>
<td>Adjust atorvastatin dose according to lipid response, but do not exceed the maximum recommended dose.</td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>↓ atorvastatin possible</td>
<td>Adjust atorvastatin dose according to lipid response, but do not exceed the maximum recommended dose.</td>
</tr>
<tr>
<td><strong>Fluvastatin</strong></td>
<td>DOR, NVP, RPV</td>
<td>↔ fluvastatin expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></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><strong>Lovastatin, Simvastatin</strong></td>
<td>DOR, RPV</td>
<td>↔ lovastatin and simvastatin expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV</td>
<td>Simvastatin AUC ↓ 68%</td>
<td>No dose adjustment needed; adjust simvastatin dose according to lipid response, but do not exceed the maximum recommended dose.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Simvastatin active metabolite AUC ↓ 60%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ETR, NVP</td>
<td>↓ lovastatin possible</td>
<td>Monitor for lovastatin toxicity.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ simvastatin possible</td>
<td></td>
</tr>
<tr>
<td><strong>Pitavastatin</strong></td>
<td>DOR, ETR, NVP, RPV</td>
<td>↔ pitavastatin expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV</td>
<td>↔ pitavastatin AUC</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td><strong>Pravastatin</strong></td>
<td>DOR, NVP, RPV</td>
<td>↔ pravastatin expected</td>
<td>No dose adjustment needed; monitor for withdrawal symptoms.</td>
</tr>
<tr>
<td></td>
<td>EFV</td>
<td>Pravastatin AUC ↓ 44%</td>
<td>Adjust pravastatin dose according to lipid response, 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><strong>Rosuvastatin</strong></td>
<td>DOR, EFV, ETR, NVP, RPV</td>
<td>↔ rosuvastatin expected</td>
<td>No dose adjustment needed.</td>
</tr>
</tbody>
</table>

### Narcotics/Treatments for Opioid Dependence

<table>
<thead>
<tr>
<th>Concomitant Drug</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>Buprenorphine Sublingual or buccal</strong></td>
<td>DOR, RPV</td>
<td>↔ buprenorphine expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV</td>
<td>Buprenorphine AUC ↓ 50%</td>
<td>No dose adjustment needed; monitor for withdrawal symptoms.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Norbuprenorphine (active metabolite) AUC ↓ 71%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>Buprenorphine AUC ↓ 25%</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>No significant effect</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td><strong>Buprenorphine Implant</strong></td>
<td>DOR, RPV</td>
<td>↔ buprenorphine expected</td>
<td>Clinical monitoring is recommended when NNRTI is initiated after insertion of buprenorphine implant.</td>
</tr>
<tr>
<td></td>
<td>EFV, ETR, NVP</td>
<td>No data</td>
<td></td>
</tr>
<tr>
<td><strong>Lofexidine</strong></td>
<td>DOR, EFV, ETR, NVP, RPV</td>
<td>↔ lofexidine expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td><strong>Methadone</strong></td>
<td>DOR, ETR</td>
<td>No significant effect</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EFV</td>
<td>Methadone AUC ↓ 52%</td>
<td>Opioid withdrawal common; monitor and increase methadone dose as necessary.</td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>Methadone AUC ↓ 37% to 51%</td>
<td>Opioid withdrawal common; monitor and increase methadone dose as necessary.</td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>R-methadone AUC ↓ 16%</td>
<td>Opioid withdrawal common; monitor and increase methadone dose as necessary.</td>
</tr>
</tbody>
</table>
Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs *(Last updated December 18, 2019; last reviewed December 18, 2019)* (page 12 of 12)

<table>
<thead>
<tr>
<th>Concomitant Drug</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>PDE5 Inhibitors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sildenafil</td>
<td>DOR</td>
<td>↔ sildenafil expected</td>
<td>No dose adjustment needed;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ sildenafil possible</td>
<td>May need to titrate sildenafil dose based on clinical effect.</td>
</tr>
<tr>
<td></td>
<td>ETR</td>
<td>Sildenafil AUC ↓ 57%</td>
<td>May need to titrate sildenafil dose based on clinical effect.</td>
</tr>
<tr>
<td></td>
<td>RPV</td>
<td>↔ sildenafil AUC and C&lt;sub&gt;max&lt;/sub&gt;</td>
<td>No dose adjustment needed;</td>
</tr>
<tr>
<td>Tadalafil</td>
<td>DOR, RPV</td>
<td>↔ tadalafil expected</td>
<td>No dose adjustment needed;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ tadalafil possible</td>
<td>May need to titrate tadalafil dose based on clinical effect.</td>
</tr>
<tr>
<td>Avanafil, Vardenafil</td>
<td>DOR, RPV</td>
<td>↔ avanafil or vardenafil expected</td>
<td>No dose adjustment needed;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ avanafil or vardenafil possible</td>
<td>May need to increase PDE5 inhibitor dose based on clinical effect.</td>
</tr>
</tbody>
</table>

* R-methadone is the active form of methadone.

**Key to Symbols:**

↑ = increase  
↓ = decrease  
↔ = no change

**Key:** ARV = antiretroviral; AUC = area under the curve; CCB = calcium channel blocker; C<sub>max</sub> = maximum plasma concentration; C<sub>min</sub> = minimum plasma concentration; DAA = direct-acting antiviral; DHA = dihydroartemisinin; DLV = delavirdine; DOR = doravirine; EFV = efavirenz; ETR = etravirine; FDA = Food and Drug Administration; HCV = hepatitis C virus; INR = international normalized ratio; MAC = *Mycobacterium avium* complex; MPA = medroxyprogesterone acetate; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; OH-itraconazole = active metabolite of itraconazole; PCP = *Pneumocystis jirovecii* pneumonia; PDE5 = phosphodiesterase type 5; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; PK = pharmacokinetic; PPI = proton pump inhibitor; RPV = rilpivirine; RTV = ritonavir
This table provides information on the known or predicted interactions between NRTIs and non-ARV drugs. 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 whether 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. In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgement to select the most appropriate alternative medication to use.

Note: Interactions associated with ddI and d4T are not included in this table. Please refer to the FDA product labels for ddI and d4T for information regarding drug interactions between these NRTIs and other drugs.

<table>
<thead>
<tr>
<th>Concomitant Drug</th>
<th>NRTI Effect on NRTI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cytomegalovirus and Hepatitis B Antivirals</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adefovir</td>
<td>TAF, TDF No data</td>
<td>Do not coadminister. Serum concentrations of TDF and/or other renally eliminated drugs may increase.</td>
</tr>
<tr>
<td>Ganciclovir, Valganciclovir</td>
<td>TAF, TDF No data</td>
<td>Serum concentrations of ganciclovir and/or TFV may increase. Monitor for dose-related toxicities.</td>
</tr>
<tr>
<td>ZDV</td>
<td>↔ ZDV expected ↔ ganciclovir expected</td>
<td>If coadministered, closely monitor for hematologic toxicities.</td>
</tr>
<tr>
<td><strong>Hepatitis C Antiviral Agents</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glecaprevir/ Pibrentasvir</td>
<td>TAF ↔ TFV AUC</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>TDF TFV AUC ↑ 29%</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>Ledipasvir/ Sofosbuvir</td>
<td>TAF TFV AUC ↑ 27%</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>TDF Ledipasvir ↑ TFV AUC 40% to 98% when TDF is given with RPV and EFV</td>
<td>Do not coadminister with EVG/c/TDF/FTC. If TDF is used in these patients, monitor for TDF toxicities. Consider using TAF in patients at risk of TDF-associated adverse events. Consider using TAF or alternative HCV therapy in patients on TDF plus a PI/r or PI/c. The safety of increased TFV exposure with this combination has not been established.</td>
</tr>
<tr>
<td></td>
<td>Ledipasvir ↑ TFV C&lt;sub&gt;max&lt;/sub&gt; 55% to 80% when TDF is given with various PIs, NNRTIs, or INSTIs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Further ↑ TFV AUC and C&lt;sub&gt;max&lt;/sub&gt; possible when TDF is given with PIs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ribavirin With Sofosbuvir 400 mg: ↔ ↔ TFV AUC</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>ZDV Ribavirin inhibits phosphorylation of ZDV</td>
<td>Consider alternative. If coadministered, closely monitor HIV virologic response and monitor for possible hematologic toxicities.</td>
</tr>
<tr>
<td>Sofosbuvir/ Velpatasvir</td>
<td>TAF ↔ TAF expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>TDF TFV C&lt;sub&gt;max&lt;/sub&gt; and AUC ↑ 39% to 81% when coadministered with various ARV combinations</td>
<td>If TDF is used in these patients, monitor for TDF-related toxicities. Consider using TAF in patients at risk of TDF-related adverse events.</td>
</tr>
<tr>
<td>Sofosbuvir/ Velpatasvir/ Voxilaprevir</td>
<td>TAF ↔ TAF expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>TDF TFV C&lt;sub&gt;max&lt;/sub&gt; and AUC ↑ 35% to 55% when coadministered with various ARV combinations</td>
<td>If TDF is used in these patients, monitor for TDF-related toxicities. Consider using TAF in patients at risk of TDF-related adverse events.</td>
</tr>
</tbody>
</table>
Table 21c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents) (Last updated December 18, 2019; last reviewed December 18, 2019) (page 2 of 3)

<table>
<thead>
<tr>
<th>Concomitant Drug</th>
<th>NRTI</th>
<th>Effect on NRTI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>INSTIs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DTG</td>
<td>TAF</td>
<td>↔ TAF AUC</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>TDF</td>
<td>↔ TDF AUC</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↔ DTG AUC</td>
<td></td>
</tr>
<tr>
<td>RAL</td>
<td>TDF</td>
<td>RAL AUC ↑ 49%</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>Narcotics and Treatment for Opioid Dependence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buprenorphine</td>
<td></td>
<td>3TC, TDF, ZDV ↔ 3TC, TDF, ZDV, and buprenorphine</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↔ DTG AUC</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TAF</td>
<td>↔ TAF expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>Methadone</td>
<td>ABC</td>
<td>Methadone clearance ↑ 22%</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>ZDV</td>
<td>ZDV AUC ↑ 29% to 43%</td>
<td>Monitor for ZDV-related adverse effects.</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbamazepine,</td>
<td>TAF</td>
<td>With Carbamazepine:</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td>oxcarbazepine,</td>
<td></td>
<td>• TAF AUC ↓ 55%</td>
<td></td>
</tr>
<tr>
<td>phenobarbital,</td>
<td></td>
<td>↓ TAF possible with other anticonvulsants</td>
<td></td>
</tr>
<tr>
<td>phenytoin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rifampin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TAF</td>
<td>TAF with Rifampin Compared with TDF Alone:</td>
<td>Do not coadminister, unless benefits outweigh risks.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• TFV-DP AUC ↑ 4.2-fold</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>TAF with Rifampin Compared with TAF Alone:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• TAF AUC ↓ 55%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• TFV-DP AUC ↓ 36%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>TAF 25 mg Twice Daily with Rifampin Compared with TAF</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Once Daily Alone:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• TAF AUC ↓ 14%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• TFV-DP AUC ↓ 24%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>TDF ↔ AUC TFV</td>
<td>No dose adjustment needed.</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>Rifabutin,</td>
<td>TAF</td>
<td>↓ TAF possible</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td>Rifapentine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>St. John's Wort</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATV (Unboosted),</td>
<td>TAF</td>
<td>TAF 10 mg with ATVr:</td>
<td>No dose adjustment needed (use TAF 25 mg).</td>
</tr>
<tr>
<td>ATV/c, ATV/r</td>
<td></td>
<td>• TAF AUC ↑ 91%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TAF 10 mg with ATV/c:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• TAF AUC ↑ 75%</td>
<td></td>
</tr>
</tbody>
</table>
### Table 21c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents) *(Last updated December 18, 2019; last reviewed December 18, 2019)* (page 3 of 3)

<table>
<thead>
<tr>
<th>Concomitant Drug</th>
<th>NRTI</th>
<th>Effect on NRTI and/or Concomitant Drug Concentrations</th>
<th>Dosing Recommendations and Clinical Comments</th>
</tr>
</thead>
</table>
| **ATV (Unboosted), ATV/c, ATV/r** | TDF  | With ATV (Unboosted):  
- ATV AUC ↓ 25% and C<sub>min</sub> ↓ 23% to 40%  
(higher C<sub>min</sub> with RTV than without RTV)  
TFV AUC ↑ 24% to 37%  
  
With ATV (Unboosted):  
- ZDV C<sub>min</sub> ↓ 30% and ↔ ZDV AUC | Do not coadminister unboosted ATV with TDF.  
Use ATV 300 mg daily plus (RTV 100 mg or COBI 150 mg) daily when coadministering TDF 300 mg daily.  
If using TDF and an H2 receptor antagonist in an ART-experienced patient, use ATV 400 mg daily plus (RTV 100 mg or COBI 150 mg) daily.  
Monitor for TDF-associated toxicities. |
| **ZDV** | | | |
| **DRV/c** | TAF  | TAF 25 mg with DRV/c:  
- ↔ TAF | No dose adjustment needed. |
| | TDF  | ↑ TFV possible | Monitor for TDF-associated toxicities. |
| **DRV/r** | TAF  | TAF 10 mg with DRV/r:  
- ↔ TAF AUC | No dose adjustment needed. |
| | TDF  | TFV AUC ↑ 22% and C<sub>min</sub> ↑ 37%  
Clinical significance unknown. If coadministered, monitor for TDF-associated toxicities. |
| **LPV/r** | TAF  | TAF 10 mg with DRV/r:  
- ↔ TAF AUC | No dose adjustment needed. |
| | TDF  | ↔ LPV/r AUC  
TFV AUC ↑ 32%  
Clinical significance unknown. If coadministered, monitor for TDF-associated toxicities. |
| **TPV/r** | ABC  | ABC AUC ↓ 35% to 44%  
Clinical significance unknown. If coadministered, monitor virologic response. |
| | TAF  | ↓ TAF expected  
Clinical significance unknown. If coadministered, monitor virologic response. |
| | TDF  | ↔ TDF AUC  
TPV AUC ↓ 9% to 18% and C<sub>min</sub> ↓ 12% to 21%  
No dose adjustment needed. |
| | ZDV  | ZDV AUC ↓ 31% to 42%  
↔ TPV AUC  
Clinical significance unknown. If coadministered, monitor virologic response. |

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

**Key:** 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; C<sub>min</sub> = minimum plasma concentration; COBI = cobicistat; d4T = stavudine; ddI = didanosine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; EVG/c = elvitegravir/cobicistat; FDA = Food and Drug Administration; FTC = emtricitabine; HCV = hepatitis C virus; INSTI = integrase strand transfer inhibitor; LPV/r = lopinavir/ritonavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TFV = tenofovir; TFV-DP = tenofovir diphosphate; TPV/r = tipranavir/ritonavir; ZDV = zidovudine
This table provides information on the known or predicted interactions between INSTIs (BIC, DTG, EVG, or RAL) and non-ARV drugs. EVG is always coadministered with COBI. For information regarding interactions between INSTIs and other ARV drugs, including dosing recommendations, refer to Tables 21c, 22a, and 22b.

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 whether 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. In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgement to select the most appropriate alternative medication to use.

### Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019)

This table provides information on the known or predicted interactions between INSTIs (BIC, DTG, EVG, or RAL) and non-ARV drugs. EVG is always coadministered with COBI. For information regarding interactions between INSTIs and other ARV drugs, including dosing recommendations, refer to Tables 21c, 22a, and 22b.

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 whether 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. In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgement to select the most appropriate alternative medication to use.

<table>
<thead>
<tr>
<th>Concomitant Drug</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>
</tbody>
</table>
| Al, Mg, +/- Ca-Containing Antacids | BIC | Al/Mg Hydroxide Antacid:  
• ↔ BIC AUC if antacid is administered 2 hours after BIC and under fasting conditions  
• BIC AUC ↓ 52% if antacid is administered 2 hours before BIC  
• BIC AUC ↓ 47% to 79% if administered simultaneously with antacid  
CaCO₃ Antacid:  
• ↔ BIC AUC if administered with food  
• BIC AUC ↓ 33% if administered under fasting conditions | With Antacids That Contain Al/Mg:  
• Administer antacids that contain Al/Mg at least 2 hours after or 6 hours before BIC.  
With Antacids That Contain Ca:  
• Administer BIC and antacids that contain Ca together with food.  
• Do not coadminister BIC simultaneously with antacids that contain Ca on an empty stomach. |
| DTG |  
DTG AUC ↓ 74% if administered simultaneously with antacid  
DTG AUC ↓ 26% if administered 2 hours before antacid  
|  
Separate DTG administration by more than 2 hours. |
| EVG/c | DTG AUC ↓ 40% to 50% if administered simultaneously with antacid  
EVG AUC ↓ 15% to 20% if administered 2 hours before or after antacid; ↔ with 4-hour interval  
|  
Separate EVG/c and antacid administration by more than 2 hours. |
| RAL | Al/Mg Hydroxide Antacid:  
• RAL Cₘᵟᵢᵣ ↓ 49% to 63%  
CaCO₃ Antacid:  
• RAL 400 mg twice daily: Cₘᵟᵢᵣ ↓ 32%  
• RAL 1,200 mg once daily: Cₘᵟᵢᵣ ↓ 48% to 57%  
| Do not coadminister RAL and Al/Mg hydroxide antacids. Use alternative acid-reducing agent.  
With CaCO₃ Antacids:  
• RAL 1,200 mg once daily: **Do not coadminister.**  
• RAL 400 mg twice daily: No dose adjustment or separation needed. |
| H2-Receptor Antagonists | BIC, DTG, EVG/c | ↔ INSTI  
|  
No dose adjustment needed. |
| RAL | RAL AUC ↑ 44% and Cₘᵞᵢᵣ ↑ 60%  
|  
No dose adjustment needed. |
### Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 2 of 17)

<table>
<thead>
<tr>
<th>Concomitant Drug</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, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Proton Pump Inhibitors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BIC, DTG, EVG/c</td>
<td>↔ INSTI</td>
<td>No dose adjustment needed.</td>
<td></td>
</tr>
<tr>
<td>RAL</td>
<td>RAL AUC ↑ 37% and C&lt;sub&gt;min&lt;/sub&gt; ↑ 24%</td>
<td>No dose adjustment needed.</td>
<td></td>
</tr>
<tr>
<td><strong>Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alfuzosin</td>
<td>BIC, DTG, RAL</td>
<td>↔ alfuzosin expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ alfuzosin expected</td>
<td>Contraindicated.</td>
<td></td>
</tr>
<tr>
<td><strong>Doxazosin</strong></td>
<td>BIC, DTG, RAL</td>
<td>↔ doxazosin expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ doxazosin possible</td>
<td>Initiate doxazosin at lowest dose and titrate based on doxazosin efficacy and adverse events. Doxazosin dose reduction may be needed.</td>
<td></td>
</tr>
<tr>
<td><strong>Tamsulosin</strong></td>
<td>BIC, DTG, RAL</td>
<td>↔ tamsulosin expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ tamsulosin expected</td>
<td>Do not coadminister, unless benefits outweigh risks. If coadministered, monitor for tamsulosin-related adverse events.</td>
<td></td>
</tr>
<tr>
<td><strong>Terazosin</strong></td>
<td>BIC, DTG, RAL</td>
<td>↔ terazosin expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ terazosin possible</td>
<td>Initiate terazosin at lowest dose and titrate based on terazosin efficacy and adverse events. Terazosin dose reduction may be necessary.</td>
<td></td>
</tr>
<tr>
<td><strong>Silodosin</strong></td>
<td>BIC, DTG, RAL</td>
<td>↔ silodosin expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ silodosin expected</td>
<td>Contraindicated.</td>
<td></td>
</tr>
<tr>
<td><strong>Antibacterials</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Antimycobacterials</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rifabutin</td>
<td>BIC</td>
<td>Rifabutin 300 mg Once Daily:</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• BIC AUC ↓ 38% and C&lt;sub&gt;min&lt;/sub&gt; ↓ 56%</td>
<td></td>
</tr>
<tr>
<td>DTG</td>
<td>Rifabutin 300 mg Once Daily:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• ↔ DTG AUC and C&lt;sub&gt;min&lt;/sub&gt; ↓ 30%</td>
<td>No dose adjustment needed.</td>
<td></td>
</tr>
<tr>
<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>
<td></td>
</tr>
<tr>
<td></td>
<td>• ↔ rifabutin AUC</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 25-O-desacetyl-rifabutin AUC ↑ 625%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• EVG AUC ↓ 21% and C&lt;sub&gt;min&lt;/sub&gt; ↓ 67%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAL</td>
<td>RAL AUC ↑ 19% and C&lt;sub&gt;min&lt;/sub&gt; ↓ 20%</td>
<td>No dose adjustment needed.</td>
<td></td>
</tr>
</tbody>
</table>
**Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019)**

<table>
<thead>
<tr>
<th>Concomitant Drug</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>Antimycobacterials, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rifampin</td>
<td>BIC</td>
<td>BIC AUC ↓ 75%</td>
<td>Contraindicated.</td>
</tr>
</tbody>
</table>
| | DTG | Rifampin with DTG 50 mg Twice Daily Compared to DTG 50 mg Twice Daily Alone:  
DTG AUC ↓ 54% and C_{min} ↓ 72%  
Rifampin with DTG 50 mg Twice Daily Compared to DTG 50 mg Once Daily Alone:  
DTG AUC ↑ 33% and C_{min} ↑ 22%  
Rifampin with DTG 50 mg Twice Daily Compared to DTG 50 mg Once Daily Alone:  
DTG AUC ↓ 54% and C_{min} ↓ 72%  
Rifampin with DTG 50 mg Twice Daily Compared to DTG 50 mg Once Daily Alone:  
DTG AUC ↑ 33% and C_{min} ↑ 22% | Use DTG 50 mg twice daily (instead of DTG 50 mg once daily) in patients without suspected or documented INSTI-associated resistance mutations.  
Consider an alternative to rifampin, such as rifabutin, in patients with certain suspected or documented INSTI-associated resistance mutations. |
| | EVG/c | Significant ↓ EVG and COBI expected | Contraindicated. |
| | RAL | RAL 400 mg:  
RAL AUC ↓ 40% and C_{min} ↓ 61%  
Rifampin with RAL 800 mg Twice Daily Compared to RAL 400 mg Twice Daily Alone:  
RAL AUC ↑ 27% and C_{min} ↓ 53%  
RAL 400 mg:  
RAL AUC ↓ 40% and C_{min} ↓ 61%  
Rifampin with RAL 800 mg Twice Daily Compared to RAL 400 mg Once Daily Alone:  
RAL AUC ↑ 27% and C_{min} ↓ 53% | Use RAL 800 mg twice daily instead of 400 mg twice daily.  
Do not coadminister RAL 1,200 mg once daily with rifampin.  
Monitor closely for virologic response, or consider using rifabutin as an alternative rifamycin. |
| | Rifapentine | BIC, DTG, EVG/c | Significant ↓ BIC, DTG, EVG, and COBI expected | Do not coadminister. |
| | RAL | Rifapentine 900 mg Once Weekly:  
RAL AUC ↑ 71% and C_{min} ↓ 12%  
Rifapentine 600 mg Once Daily:  
RAL C_{min} ↓ 41% | For once-weekly rifapentine and RAL 400 mg twice daily, no dose adjustment needed.  
Do not coadminister with once-daily rifapentine. |
| **Macrolides** | | | |
| Azithromycin | All INSTIs | ↔ azithromycin expected | No dose adjustment needed. |
| Clarithromycin | BIC | ↑ BIC possible | No dose adjustment needed. |
| | DTG, RAL | ↔ clarithromycin expected | No dose adjustment needed. |
| | EVG/c | ↑ clarithromycin expected  
↑ COBI possible | Reduce clarithromycin dose by 50% in patients with CrCl 50 to 60 mL/min.  
Do not coadminister in patients with CrCl <50 mL/min.  
Consider alternative ARV or use azithromycin. |
| | RAL | ↑ clarithromycin expected  
↑ COBI possible | No data available for dose recommendation.  
Consider alternative ARV or use azithromycin. |
| Erythromycin | BIC | ↑ BIC possible | No dose adjustment needed. |
| | DTG, RAL | ↔ INSTI expected  
↔ erythromycin expected | No dose adjustment needed. |
| | EVG/c | ↑ erythromycin expected  
↑ COBI possible | No data available for dose recommendation.  
Consider alternative ARV or use azithromycin. |
| **Anticoagulants** | | | |
| Apixaban | BIC, DTG, RAL | ↔ apixaban expected | No dose adjustment needed. |
| | EVG/c | ↑ apixaban expected | Do not coadminister in patients who require apixaban 2.5 mg twice daily.  
Reduce apixaban dose by 50% in patients who require apixaban 5 mg or 10 mg twice daily. |
<table>
<thead>
<tr>
<th>Concomitant Drug</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>Betrixaban</td>
<td>BIC, DTG, RAL</td>
<td>↔ betrixaban expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ betrixaban expected</td>
<td>Administer initial single dose of betrixaban 80 mg, followed by betrixaban 40 mg once daily.</td>
<td></td>
</tr>
<tr>
<td>Dabigatran</td>
<td>BIC, DTG, RAL</td>
<td>↔ dabigatran expected</td>
<td>No dose adjustment needed.</td>
</tr>
</tbody>
</table>
| EVG/c            | ↑ dabigatran expected | **With COBI 150 mg Alone:**  
• Dabigatran AUC ↑ 110% to 127%  
Dabigatran dosing recommendation depends on indication and renal function. Refer to dabigatran prescribing information for dosing instructions when using dabigatran concomitantly with P-glycoprotein inhibitors. |
| Edoxaban         | BIC, DTG, RAL | ↔ edoxaban expected | No dose adjustment needed. |
| EVG/c            | ↔ or ↑ edoxaban expected | **Stroke Prevention in Nonvalvular Atrial Fibrillation:**  
• No dose adjustment needed.  
**Deep Venous Thrombosis and Pulmonary Embolism:**  
• Administer edoxaban 30 mg once daily. |
| Rivaroxaban      | BIC, DTG, RAL | ↔ rivaroxaban expected | No dose adjustment needed. |
| EVG/c            | ↑ rivaroxaban expected | **Do not coadminister.** |
| Warfarin         | BIC, DTG, RAL | ↔ warfarin expected | No dose adjustment needed. |
| EVG/c            | ↑ or ↓ warfarin possible | Monitor INR and adjust warfarin dose accordingly. |

**Anticonvulsants**

<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>Carbamazepine</td>
<td>BIC</td>
<td>↓ BIC possible</td>
</tr>
</tbody>
</table>
| DTG   | DTG AUC ↓ 49% | Increase DTG dose to 50 mg twice daily in ART-naive or ART-experienced, INSTI-naive patients.  
**Do not coadminister in INSTI-experienced patients with known or suspected INSTI resistance.** |
| EVG/c | Carbamazepine AUC ↑ 43%  
EVG AUC ↓ 69% and Cmin ↓ >99%  
↓ COBI expected | **Contraindicated.** |
| RAL   | ↓ or ↔ RAL possible | **Do not coadminister.** |
| Eslicarbzepine | All INSTIs | ↓ INSTI possible  
↓ COBI possible | Consider alternative ARV or anticonvulsant. |
<table>
<thead>
<tr>
<th>Concomitant Drug</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>Anticonvulsants, continued</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethosuximide</td>
<td>BIC, DTG, RAL</td>
<td>↔ ethosuximide expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EVG/c</td>
<td>↑ ethosuximide possible</td>
<td>Monitor for ethosuximide-related adverse events.</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>BIC, DTG, RAL</td>
<td>↔ lamotrigine expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EVG/c</td>
<td>No data</td>
<td>Monitor anticonvulsant concentrations and adjust dose accordingly.</td>
</tr>
<tr>
<td>Oxcarbazepine</td>
<td>BIC, DTG</td>
<td>↓ BIC and DTG possible</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
<tr>
<td></td>
<td>DTG</td>
<td>↓ DTG possible</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
<tr>
<td></td>
<td>EVG/c</td>
<td>↓ EVG/c and RAL possible</td>
<td><strong>Contraindicated.</strong></td>
</tr>
<tr>
<td></td>
<td>RAL</td>
<td>↓ or ↔ RAL possible</td>
<td><strong>Do not coadminister.</strong></td>
</tr>
<tr>
<td>Valproic Acid</td>
<td>All INSTIs</td>
<td>No data</td>
<td>Monitor valproic acid concentration and virologic response.</td>
</tr>
<tr>
<td>Antidepressants, Anxiolytics, Antipsychotics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>BIC, DTG, RAL</td>
<td>↔ aripiprazole expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EVG/c</td>
<td>↑ aripiprazole expected</td>
<td>Administer 25% of the usual aripiprazole dose. Titrate based on aripiprazole efficacy and adverse events. Refer to aripiprazole label for dosing recommendations in patients who are known to be CYP2D6 poor metabolizers or who have major depressive disorder.</td>
</tr>
<tr>
<td>Brexpiprazole</td>
<td>BIC, DTG, RAL</td>
<td>↔ brexpiprazole expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EVG/c</td>
<td>↑ brexpiprazole expected</td>
<td>Administer 25% of the usual brexpiprazole dose. Titrate based on brexpiprazole efficacy and adverse events. Refer to brexpiprazole label for dosing recommendations in patients who are known to be CYP2D6 poor metabolizers or who have major depressive disorder.</td>
</tr>
<tr>
<td>Bupropion</td>
<td>BIC, DTG, RAL</td>
<td>↔ bupropion expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EVG/c</td>
<td>↑ bupropion possible</td>
<td>Titrate bupropion dose based on clinical response.</td>
</tr>
<tr>
<td>Buspirone</td>
<td>BIC, DTG, RAL</td>
<td>↔ buspirone expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EVG/c</td>
<td>↑ buspirone possible</td>
<td>Initiate buspirone at a low dose. Buspirone dose reduction may be needed.</td>
</tr>
</tbody>
</table>
### Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019)

#### Concomitant Drug, Antidepressants, Anxiolytics, Antipsychotics, continued

<table>
<thead>
<tr>
<th>Concomitant Drug</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>Cariprazine</td>
<td>BIC, DTG, RAL</td>
<td>↔ cariprazine expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ cariprazine expected</td>
<td><strong>Starting Cariprazine in a Patient Who Is Already Receiving EVG/c:</strong>&lt;br&gt;• Administer cariprazine 1.5 mg on Day 1 and Day 3, with no dose given on Day 2. From Day 4 onward, administer cariprazine 1.5 mg daily. Dose can be increased to a maximum dose of 3 mg daily. If EVG/c is withdrawn, cariprazine dose may need to be increased.</td>
<td></td>
</tr>
<tr>
<td>Iloperidone</td>
<td>BIC, DTG, RAL</td>
<td>↔ iloperidone expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ iloperidone expected</td>
<td><strong>Decrease iloperidone dose by 50%</strong>.</td>
<td></td>
</tr>
<tr>
<td>Lurasidone</td>
<td>BIC, DTG, RAL</td>
<td>↔ lurasidone expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ lurasidone expected</td>
<td><strong>Contraindicated.</strong></td>
<td></td>
</tr>
<tr>
<td>Nefazodone</td>
<td>BIC, DTG, RAL</td>
<td>↔ nefazodone expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ nefazodone expected</td>
<td><strong>Consider alternative ARV or antidepressant.</strong></td>
<td></td>
</tr>
<tr>
<td>Pimavanserin</td>
<td>BIC, DTG, RAL</td>
<td>↔ pimavanserin expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ pimavanserin expected</td>
<td><strong>Reduce pimavanserin dose to 10 mg.</strong></td>
<td></td>
</tr>
<tr>
<td>Pimozide</td>
<td>BIC, DTG, RAL</td>
<td>↔ quetiapine expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ quetiapine AUC expected</td>
<td><strong>Starting Quetiapine in a Patient Receiving EVG/c:</strong>&lt;br&gt;• Start quetiapine at the lowest dose and titrate up as needed. Monitor for quetiapine efficacy and adverse events. &lt;br&gt;&lt;br&gt;<strong>Starting EVG/c in a Patient Receiving a Stable Dose of Quetiapine:</strong>&lt;br&gt;• Reduce quetiapine dose to 1/6 of the current dose, and closely monitor for quetiapine efficacy and adverse events.</td>
<td></td>
</tr>
</tbody>
</table>
### Concomitant Drug, INSTI, Effect on INSTI or Concomitant Drug Concentrations, Dosing Recommendations and Clinical Comments

#### Concomitant Drug

**Antidepressants, Anxiolytics, Antipsychotics**, continued

Also see Sedative/Hypnotics section below

#### Selective Serotonin Reuptake Inhibitors

Citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline

- **EVG/c**
  - ↔ EVG
  - ↔ sertraline
  - ↑ other SSRIs possible
  - No dose adjustment needed.

- **BIC, DTG, RAL**
  - ↔ BIC, DTG and RAL expected
  - ↔ SSRI expected
  - No dose adjustment needed.

#### Tricyclic Antidepressants

Amitriptyline, desipramine, doxepin, imipramine, nortriptyline

- **EVG/c**
  - Desipramine AUC ↑ 65%
  - ↑ TCA expected
  - Initiate with lowest dose of TCA and titrate dose carefully.

- **BIC, DTG, RAL**
  - ↔ TCA expected
  - No dose adjustment needed.

#### Trazodone

- **BIC, DTG, RAL**
  - ↔ trazodone expected
  - No dose adjustment needed.

- **EVG/c**
  - ↑ trazodone possible
  - Initiate with lowest dose of trazodone and titrate dose carefully.

#### Ziprasidone

- **BIC, DTG, RAL**
  - ↔ ziprasidone expected
  - No dose adjustment needed.

- **EVG/c**
  - ↑ ziprasidone possible
  - Monitor for ziprasidone-related adverse events.

#### Other Antipsychotics

CYP3A4 and/or CYP2D6 substrates (e.g., perphenazine, risperidone, thioridazine)

- **EVG/c**
  - ↑ antipsychotic possible
  - Initiate antipsychotic at a low dose. Antipsychotic dose reduction may be needed.

#### Antifungals

- **Isavuconazole**
  - **BIC**
    - ↑ BIC possible
    - No dose adjustment needed.

  - **EVG/c**
    - ↑ isavuconazole expected
      - or ↓ EVG and COBI possible
      - If coadministered, consider monitoring isavuconazole concentrations and assessing virologic response.

- **Itraconazole**
  - **BIC**
    - ↑ BIC expected
    - No dose adjustment needed.

  - **DTG, RAL**
    - ↔ INSTI expected
      - ↔ itraconazole expected
      - No dose adjustment needed.

  - **EVG/c**
    - ↑ itraconazole expected
      - ↑ EVG and COBI possible
      - Consider monitoring itraconazole concentrations to guide dose adjustments. Do not coadminister with high itraconazole doses (>200 mg/day) unless guided by itraconazole concentrations.
Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019)  
(page 8 of 17)

<table>
<thead>
<tr>
<th>Concomitant Drug</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>Antifungals, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posaconazole</td>
<td>BIC</td>
<td>↑ BIC expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>DTG, RAL</td>
<td>↔ INSTI expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↔ posaconazole expected</td>
<td></td>
</tr>
<tr>
<td></td>
<td>EVG/c</td>
<td>↑ EVG and COBI possible</td>
<td>If coadministered, monitor posaconazole</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ posaconazole possible</td>
<td>concentrations.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Voriconazole</td>
<td>BIC</td>
<td>↑ BIC possible</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>DTG, RAL</td>
<td>↔ INSTI expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↔ voriconazole expected</td>
<td></td>
</tr>
<tr>
<td></td>
<td>EVG/c</td>
<td>↑ voriconazole expected</td>
<td>Do not coadminister voriconazole and COBI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ EVG and COBI possible</td>
<td>unless benefit outweighs risk.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>If coadministered, consider monitoring</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>voriconazole concentrations and adjust dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>accordingly.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Antihyperglycemics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metformin</td>
<td>BIC</td>
<td>Metformin AUC ↑ 39%</td>
<td>Monitor for adverse events of metformin.</td>
</tr>
<tr>
<td></td>
<td>DTG</td>
<td>DTG 50 mg Once Daily plus Metformin 500 mg Twice</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Daily:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Metformin AUC ↑ 79% and C&lt;sub&gt;max&lt;/sub&gt; ↑ 66%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>DTG 50 mg Twice Daily plus Metformin 500 mg Twice</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Daily:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Metformin AUC ↑ 2.4-fold and C&lt;sub&gt;max&lt;/sub&gt; ↑</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2-fold</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RAL</td>
<td>↔ metformin expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>Saxagliptin</td>
<td>BIC, DTG, RAL</td>
<td>↔ saxagliptin expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></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>BIC, DTG, RAL</td>
<td>↔ dapagliflozin or saxagliptin expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EVG/c</td>
<td>↑ saxagliptin expected</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td>Antiplatelets</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>BIC, DTG, RAL</td>
<td>↔ clopidogrel expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EVG/c</td>
<td>↓ clopidogrel active metabolite, with impaired</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>platelet inhibition expected</td>
<td></td>
</tr>
<tr>
<td>Prasugrel</td>
<td>BIC, DTG, RAL</td>
<td>↔ prasugrel expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EVG/c</td>
<td>↓ prasugrel active metabolite, with no impairment</td>
<td>Insufficient data to make a dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>of platelet inhibition expected</td>
<td>recommendation.</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](https://aidsinfo.nih.gov/guidelines) on 7/3/2020
Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs  *(Last updated December 18, 2019; last reviewed December 18, 2019)*  (page 9 of 17)

<table>
<thead>
<tr>
<th>Concomitant Drug</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>Antiplatelets, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ticagrelor</td>
<td>BIC, DTG, RAL</td>
<td>↔ ticagrelor expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ ticagrelor expected</td>
<td>Do not coadminister.</td>
<td></td>
</tr>
<tr>
<td>Vorapaxar</td>
<td>BIC, DTG, RAL</td>
<td>↔ vorapaxar expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ vorapaxar expected</td>
<td>Do not coadminister.</td>
<td></td>
</tr>
<tr>
<td><strong>Beta-Agonists, Long-Acting Inhaled</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arformoterol, Formoterol</td>
<td>All INSTIs</td>
<td>↔ arformoterol or formoterol expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>Indacaterol</td>
<td>BIC, DTG, RAL</td>
<td>↔ indacaterol expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ indacaterol expected</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Olodaterol</td>
<td>BIC, DTG, RAL</td>
<td>↔ olodaterol expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ olodaterol expected</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salmeterol</td>
<td>BIC, DTG, RAL</td>
<td>↔ salmeterol expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ salmeterol possible</td>
<td>Do not coadminister because of potential increased risk of salmeterol-associated cardiovascular events.</td>
<td></td>
</tr>
<tr>
<td><strong>Cardiac Medications</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amiodarone</td>
<td>BIC, DTG, RAL</td>
<td>↔ INSTI expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↔ amiodarone expected</td>
<td></td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ INSTI possible</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ amiodarone possible</td>
<td></td>
</tr>
<tr>
<td>Bepridil, Digoxin, Disopyramide, Dronedarone, Flecaïnide, Systemic Lidocaine, Mexilitine, Propafenone, Quinidine</td>
<td>BIC, DTG</td>
<td>↔ expected for the listed antiarrhythmics, except for disopyramide</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ disopyramide possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RAL</td>
<td>↔ expected for the listed antiarrhythmics</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EVG/c</td>
<td>↑ antiarrhythmics possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Digoxin C_{max} ↑ 41% and ↔ AUC</td>
<td>Therapeutic drug monitoring for antiarrhythmics, if available, is recommended.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beta-Blockers (e.g., metoprolol, timolol)</td>
<td>BIC, DTG, RAL</td>
<td>↔ beta-blocker expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EVG/c</td>
<td>↑ beta-blocker possible</td>
<td>Beta-blocker dose may need to be decreased; adjust dose based on clinical response.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Consider using an alternative ARV, or a beta-blocker that is not metabolized by CYP450 enzymes (e.g., atenolol, labetalol, nadolol, sotalol).</td>
</tr>
</tbody>
</table>
### Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 10 of 17)

<table>
<thead>
<tr>
<th>Concomitant Drug</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>Cardiac Medications, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bosentan</td>
<td>BIC, DTG</td>
<td>↓ BIC and DTG possible</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>RAL</td>
<td>↔ bosentan expected</td>
<td>No dose adjustment needed.</td>
</tr>
</tbody>
</table>
| | EVG/c | ↑ bosentan possible | **In Patients on EVG/c ≥10 Days:**
| | | | • Start bosentan at 62.5 mg once daily or every other day based on individual tolerability. |
| | | | **In Patients on Bosentan Who Require EVG/c:**
| | | | • Stop bosentan ≥36 hours before EVG/c initiation. At least 10 days after initiation of EVG/c, resume bosentan at 62.5 mg once daily or every other day based on individual tolerability. |
| Calcium Channel Blockers | BIC | ↑ BIC possible with diltiazem
| | | ↔ expected for all other CCBs | No dose adjustment needed. |
| | DTG, RAL | ↔ INSTI expected
| | | ↔ CCB expected | No dose adjustment needed. |
| | EVG/c | ↑ CCB possible | Titrate CCB dose and monitor for CCB efficacy and adverse events. |
| Dofetilide | BIC, DTG | ↑ dofetilide expected | **Contraindicated.** |
| | RAL | ↔ dofetilide expected | No dose adjustment needed. |
| | EVG/c | ↑ dofetilide possible | **Do not coadminister.** |
| Eplerenone | BIC, DTG, RAL | ↔ eplerenone expected | No dose adjustment needed. |
| | EVG/c | ↑ eplerenone expected | **Contraindicated.** |
| Ivabradine | BIC, DTG, RAL | ↔ ivabradine expected | No dose adjustment needed. |
| | EVG/c | ↑ ivabradine expected | **Contraindicated.** |
| Ranolazine | BIC, DTG, RAL | ↔ ranolazine expected | No dose adjustment needed. |
| | EVG/c | ↑ ranolazine expected | **Contraindicated.** |
| **Corticosteroids** | | | |
| Beclomethasone, Budesonide, Ciclesonide, Fluticasone, Mometasone | BIC, DTG, EVG/c, RAL | ↔ glucocorticoid expected | No dose adjustment needed. |
| Inhaled or intranasal | | | | |
| **Do not coadminister unless potential benefits of inhaled or intranasal corticosteroid outweigh the risks of systemic corticosteroid adverse effects. Coadministration can result in adrenal insufficiency and Cushing's syndrome. Consider using an alternative corticosteroid (e.g., beclomethasone).** |
### Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

**Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019)**

<table>
<thead>
<tr>
<th>Concomitant Drug</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>Corticosteroids, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Betamethasone, Budesonide Systemic | BIC, DTG, RAL | ↔ INSTI expected  
↔ glucocorticoid expected | No dose adjustment needed.  
Do not coadminister unless potential benefits of systemic budesonide outweigh the risks of systemic corticosteroid adverse effects. Coadministration can result in adrenal insufficiency and Cushing’s syndrome. |
|  
EVG/c | ↑ glucocorticoids possible  
↓ EVG possible | Consider alternative corticosteroid for long-term use or alternative ARV. If coadministration is necessary, monitor virologic response to ART.  
Coadministration may be considered if the potential benefits outweigh the risks of systemic corticosteroid adverse effects. If coadministration is necessary, monitor for adrenal insufficiency and Cushing’s syndrome. |
| Dexamethasone Systemic | BIC | ↓ BIC possible | No dose adjustment needed.  
Consider alternative corticosteroid for long-term use or alternative ARV. If coadministration is necessary, monitor virologic response to ART. |
|  
DTG, RAL | ↔ INSTI expected | No dose adjustment needed.  
Consider alternative corticosteroid for long-term use or alternative ARV. If coadministration is necessary, monitor virologic response to ART. |
|  
EVG/c | ↓ EVG and COBI possible | No dose adjustment needed.  
Consider alternative corticosteroid for long-term use or alternative ARV. If coadministration is necessary, monitor virologic response to ART. |
| Prednisone, Prednisolone Systemic | BIC, DTG, RAL | ↔ glucocorticoid expected | No dose adjustment needed.  
No dose adjustment needed.  
Coadministration may be considered if the potential benefits outweigh the risks of systemic corticosteroid adverse effects. If coadministration is necessary, monitor for adrenal insufficiency and Cushing’s syndrome. |
|  
EVG/c | ↑ prednisolone possible | No dose adjustment needed.  
Coadministration may be considered if the potential benefits outweigh the risks of systemic corticosteroid adverse effects. If coadministration is necessary, monitor for adrenal insufficiency and Cushing’s syndrome. |
| Betamethasone, Methylprednisolone, Prednisolone, Triamcinolone Local injections, including intra-articular, epidural, or intra-orbital | BIC, DTG, RAL | ↔ glucocorticoid expected | No dose adjustment needed.  
No dose adjustment needed.  
Do not coadminister.  
Coadministration may result in adrenal insufficiency and Cushing’s syndrome. |
|  
EVG/c | ↑ glucocorticoid expected | No dose adjustment needed.  
Decrease daclatasvir dose to 30 mg once daily. |
| **Hepatitis C Direct-Acting Antiviral Agents** |
| Daclatasvir | BIC, RAL | No data | No dose adjustment needed. |
|  
DTG | ↔ daclatasvir | No dose adjustment needed. |
|  
EVG/c | ↑ daclatasvir | Decrease daclatasvir dose to 30 mg once daily. |
| Dasabuvir plus Ombitasvir/Paritaprevir/RTV | BIC, DTG | No data | No dose adjustment needed.  
**Do not coadminister.** |
|  
EVG/c | No data | No dose adjustment needed. |
|  
RAL | RAL AUC ↑ 134% | No dose adjustment needed. |
| Elbasvir/Grazoprevir | BIC | ↔ BIC expected | No dose adjustment needed. |
|  
DTG | ↔ elbasvir  
↔ grazoprevir  
↔ DTG | No dose adjustment needed. |
<table>
<thead>
<tr>
<th>Concomitant Drug</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>Hepatitis C Direct-Acting Antiviral Agents, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elbasvir/Grazoprevir</td>
<td>EVG/c</td>
<td>↑ elbasvir expected</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ grazoprevir expected</td>
<td></td>
</tr>
<tr>
<td>RAL</td>
<td></td>
<td>↔ elbasvir</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↔ grazoprevir</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>↔ RAL with elbasvir</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>RAL AUC ↑ 43% with grazoprevir</td>
<td></td>
</tr>
<tr>
<td>Gilecaprevir/Pibrentasvir</td>
<td>BIC</td>
<td>↔ BIC expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>DTG, RAL</td>
<td>No significant effect</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EVG/c</td>
<td>Gilecaprevir AUC ↑ 3-fold</td>
<td>No dose adjustment needed. If coadministered with TDF, monitor for TDF-related adverse events. Consider monitoring for hepatotoxicity if coadministered with TDF or TAF.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pibrentasvir AUC ↑ 57%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>EVG AUC ↑ 47%</td>
<td></td>
</tr>
<tr>
<td>Ledipasvir/Sofosbuvir</td>
<td>BIC, DTG, RAL</td>
<td>↔ DTG and RAL</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EVG/c/TDF/FTC</td>
<td>↑ TDF expected</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ ledipasvir expected</td>
<td></td>
</tr>
<tr>
<td></td>
<td>EVG/c/TAF/FTC</td>
<td>↔ EVG/c/TAF/FTC expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>Sofosbuvir</td>
<td>All INSTIs</td>
<td>↔ INSTI expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↔ sofosbuvir expected</td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir/Velpatasvir</td>
<td>All INSTIs</td>
<td>↔ INSTI expected</td>
<td>No dose adjustment needed. If coadministered with TDF, monitor for TDF-related adverse events.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↔ sofosbuvir and velpatasvir expected</td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir/Velpatasvir/Voxilaprevir</td>
<td>EVG/c</td>
<td>When Administered with Sofosbuvir/Velpatasvir/Voxilaprevir (400 mg/100 mg/100 mg) plus Voxilaprevir 100 mg:</td>
<td>Do not dose adjustment needed. If coadministered with TDF, monitor for TDF-related adverse events. Consider monitoring for hepatotoxicity if coadministered with TDF or TAF.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Sofosbuvir AUC ↑ 22%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• ↔ velpatasvir</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Voxilaprevir AUC ↑ 2-fold</td>
<td></td>
</tr>
<tr>
<td></td>
<td>BIC, DTG, RAL</td>
<td>↔ INSTI expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↔ sofosbuvir, velpatasvir, and voxilaprevir expected</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>BIC, DTG</td>
<td>↓ BIC and DTG possible</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td>EVG/c</td>
<td>↓ EVG and COBI expected</td>
<td>Contraindicated.</td>
</tr>
<tr>
<td><strong>Hormonal Therapies</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contraceptives: Non-Oral</td>
<td>All INSTIs</td>
<td>No data</td>
<td>No drug-drug interaction studies have been conducted with INSTIs and non-oral routes of hormone administration. It is unclear whether drug-drug interaction data for oral drugs can be used to predict interactions for non-oral drugs.</td>
</tr>
<tr>
<td>Concomitant Drug</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>Contraceptives – Oral</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hormonal Therapies, continued</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BIC, DTG, RAL</td>
<td></td>
<td>++ ethinyl estradiol and norgestimate</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td></td>
<td>++ INSTI</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Norgestimate AUC, Cmax, and Cmin ↑ &gt;2-fold</td>
<td>The effects of increases in progestin (norgestimate) are not fully known and may include insulin resistance, dyslipidemia, acne, and venous thrombosis. Weigh the risks and benefits of using the drug and consider using an alternative ARV or contraceptive method.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ethinyl estradiol AUC ↓ 25% and Cmin ↓ 44%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ drospirenone possible</td>
<td>Clinical monitoring is recommended, due to the potential for hyperkalemia. Consider using alternative ARV or contraceptive method.</td>
</tr>
<tr>
<td>Gender-Affirming Therapy</td>
<td>BIC, DTG, EVG/c, RAL</td>
<td>++ estrogen expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>++ testosterone expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EVG/c</td>
<td>↓ or ↑ estradiol possible</td>
<td>Adjust dutasteride dose as needed based on clinical effects and endogenous hormone concentrations.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ dutasteride and finasteride possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ testosterone possible</td>
<td>Monitor masculinizing effects of testosterone and monitor for adverse effects. Adjust testosterone dose as necessary.</td>
</tr>
<tr>
<td>Menopausal Replacement Therapy</td>
<td>BIC, DTG, RAL</td>
<td>↔ estrogen expected with estradiol or conjugated estrogen (equine and synthetic)</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↔ drospirenone, medroxyprogesterone, and micronized progesterone expected</td>
<td></td>
</tr>
<tr>
<td></td>
<td>EVG/c</td>
<td>↓ or ↑ estrogen possible</td>
<td>Adjust estrogen and progestin dose as needed based on clinical effects.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ drospirenone possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ oral medroxyprogesterone possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ oral micronized progesterone possible</td>
<td></td>
</tr>
<tr>
<td>Immunosuppressants</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyclosporine, Everolimus, Sirolimus, Tacrolimus</td>
<td>BIC, DTG, RAL</td>
<td>↔ immunosuppressant expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EVG/c</td>
<td>↑ immunosuppressant possible</td>
<td>Initiate with an adjusted dose of immunosuppressant to account for potential increased concentrations of the immunosuppressant and monitor for immunosuppressant-related adverse events. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with a specialist as necessary.</td>
</tr>
<tr>
<td>Lipid-Modifying Agents</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>BIC, DTG, RAL</td>
<td>↔ atorvastatin expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>EVG/c</td>
<td>Atorvastatin AUC ↑ 2.6-fold and Cmax ↑ 2.3-fold</td>
<td>Titrate statin dose carefully and administer the lowest effective dose while monitoring for adverse events. Do not exceed 20 mg atorvastatin daily.</td>
</tr>
</tbody>
</table>
Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019) (page 14 of 17)

<table>
<thead>
<tr>
<th>Concomitant Drug</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>Lipid-Modifying Agents</strong>, continued</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lomitapide</td>
<td>BIC, DTG, RAL</td>
<td>↔ lomitapide expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ lomitapide expected</td>
<td><strong>Contraindicated.</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>BIC, DTG, RAL</td>
<td>↔ lovastatin expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>Significant ↑ lovastatin expected</td>
<td><strong>Contraindicated.</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>BIC, DTG, RAL</td>
<td>↔ statin expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>No data</td>
<td>No data available for dose recommendation.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>BIC, DTG, RAL</td>
<td>↔ rosuvastatin expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<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 effective dose while monitoring for adverse events.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>BIC, DTG, RAL</td>
<td>↔ simvastatin expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>Significant ↑ simvastatin expected</td>
<td><strong>Contraindicated.</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>BIC, DTG, RAL</td>
<td>↔ buprenorphine and norbuprenorphine (active metabolite) expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>Buprenorphine AUC ↑ 35% and C&lt;sub&gt;min&lt;/sub&gt; ↑ 66%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Norbuprenorphine (active metabolite) AUC ↑ 42% and C&lt;sub&gt;min&lt;/sub&gt; ↑ 57%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>↔ buprenorphine or norbuprenorphine (active metabolite) expected (sublingual)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>↔ buprenorphine or norbuprenorphine (active metabolite) expected (implant)</td>
<td>No dose adjustment needed.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>BIC, DTG, RAL</td>
<td>↑ fentanyl</td>
<td>Monitor for fentanyl efficacy and adverse events, including potentially fatal respiratory depression.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ lofexidine</td>
<td>Monitor for lofexidine-related adverse events, including symptoms of orthostasis and bradycardia.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>BIC, DTG, RAL</td>
<td>↔ methadone</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>BIC, DTG, RAL</td>
<td>↑ tramadol and M1 (active metabolite) expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ trabamil expected</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓ M1 (active metabolite) possible</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>BIC, DTG, RAL</td>
<td>↑ tramadol expected</td>
<td></td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ tramadol expected</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓ M1 (active metabolite) possible</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>BIC, DTG, RAL</td>
<td>↑ tramadol expected</td>
<td></td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ tramadol expected</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓ M1 (active metabolite) possible</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV 108

Downloaded from https://aidsinfo.nih.gov/guidelines on 7/3/2020
### Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs  
(Last updated December 18, 2019; last reviewed December 18, 2019)  
(page 15 of 17)

<table>
<thead>
<tr>
<th>Concomitant Drug</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</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avanafil</td>
<td>BIC, DTG, RAL</td>
<td>↔ avanafil expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>No data</td>
<td></td>
<td><strong>Do not coadminister.</strong></td>
</tr>
<tr>
<td>Sildenafil</td>
<td>BIC, DTG, RAL</td>
<td>↔ sildenafil expected</td>
<td>No dose adjustment needed.</td>
</tr>
</tbody>
</table>
| EVG/c            | ↑ sildenafil expected | | For Treatment of Erectile Dysfunction:  
|                  |                  | • Start with sildenafil 25 mg every 48 hours  
|                  |                  | and monitor for adverse effects of sildenafil.  
|                  |                  | **Contraindicated for treatment of PAH.** |
| Tadalafil        | BIC, DTG, RAL | ↔ tadalafil expected | No dose adjustment needed. |
| EVG/c            | ↑ tadalafil expected | | For Treatment of Erectile Dysfunction:  
|                  |                  | • Start with tadalafil 5 mg and do not exceed a  
|                  |                  | single dose of tadalafil 10 mg every 72 hours.  
|                  |                  | Monitor for adverse effects of tadalafil.  
|                  |                  | For Treatment of PAH  
|                  |                  | In Patients on EVG/c >7 Days:  
|                  |                  | • Start with tadalafil 20 mg once daily and  
|                  |                  | increase to tadalafil 40 mg once daily based  
|                  |                  | on tolerability.  
|                  |                  | In Patients on Tadalafil who Require EVG/c:  
|                  |                  | • Stop tadalafil ≥24 hours before EVG/c  
|                  |                  | initiation. Seven days after EVG/c initiation,  
|                  |                  | restart tadalafil at 20 mg once daily, and  
|                  |                  | increase to tadalafil 40 mg once daily based  
|                  |                  | on tolerability.  
|                  |                  | In Patients on Tadalafil who Require EVG/c:  
|                  |                  | • Start with vardenafil 2.5 mg every 72 hours  
|                  |                  | and monitor for adverse effects of vardenafil.  
| Vardenafil       | BIC, DTG, RAL | ↔ vardenafil expected | No dose adjustment needed. |
| EVG/c            | ↑ vardenafil expected | | For Treatment of Erectile Dysfunction:  
|                  |                  | • Start with vardenafil 2.5 mg every 72 hours  
|                  |                  | and monitor for adverse effects of vardenafil.  
|                  |                  | Start with vardenafil 2.5 mg every 72 hours  
|                  |                  | and monitor for adverse effects of vardenafil.  
| Sedative/Hypnotics |       |                                                   |                                             |
| **Buspirone**    | BIC, DTG, RAL | ↔ buspirone expected | No dose adjustment needed. |
| EVG/c            | ↑ buspirone expected | | **Initiate buspirone at a low dose. Dose  
|                  |                  | reduction may be needed.** |
| **Clonazepam,  
|                  |                  |                                     | Dose reduction of benzodiazepine may be  
|                  |                  |                                     | necessary. Initiate with a low dose and monitor  
|                  |                  |                                     | for benzodiazepine-related adverse events.  
|                  |                  |                                     | Consider using an alternative  
|                  |                  |                                     | benzodiazepine, such as lorazepam,  
|                  |                  |                                     | oxazepam, or temazepam.  
|                  |                  |                                     |                                     |
| Midazolam,  
|                  |                  |                                     |                                     |
|                  | BIC, RAL | ↔ benzodiazepine expected | No dose adjustment needed. |

*Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV*  
109

Downloaded from [https://aidsinfo.nih.gov/guidelines](https://aidsinfo.nih.gov/guidelines) on 7/3/2020
<table>
<thead>
<tr>
<th>Sedative/Hypnotics, continued</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Concomitant Drug</strong></td>
<td><strong>INSTI</strong></td>
<td><strong>Effect on INSTI or Concomitant Drug Concentrations</strong></td>
<td><strong>Dosing Recommendations and Clinical Comments</strong></td>
</tr>
</tbody>
</table>
| **Midazolam, Triazolam, continued** | DTG | With DTG 25 mg:  
• ↔ midazolam AUC  
↑ triazolam expected | No dose adjustment needed.  
Contraindicated. Do not coadminister triazolam or oral midazolam and EVG/c.  
Parenteral midazolam can be administered in a closely monitored setting. Consider dose reduction, especially if >1 dose is administered. |
|  | EVG/c | ↑ midazolam expected  
↑ triazolam expected |  |
| **Suvorexant** | BIC, DTG, RAL | ↔ suvorexant expected | No dose adjustment needed.  
Do not coadminister. |
|  | EVG/c | ↑ suvorexant expected |  |
| **Zolpidem** | BIC, DTG, RAL | ↔ zolpidem expected | No dose adjustment needed.  
Initiate zolpidem at a low dose. Dose reduction of zolpidem may be necessary. |
|  | EVG/c | ↑ zolpidem expected |  |
| **Miscellaneous Drugs** |  |  |  |
| **Calcifediol** | BIC, DTG, RAL | ↔ calcifediol expected | No dose adjustment needed.  
Dose adjustment of calcifediol may be required. Monitor serum 25-hydroxyvitamin D, intact PTH, and serum Ca concentrations. |
|  | EVG/c | ↑ calcifediol expected |  |
| **Cisapride** | BIC, DTG, RAL | ↔ cisapride expected | No dose adjustment needed.  
Contraindicated. |
|  | EVG/c | ↑ cisapride expected |  |
| **Colchicine** | BIC, DTG, RAL | ↔ colchicine expected | No dose adjustment needed.  
Do not coadminister in patients with hepatic or renal impairment.  
**For Treatment of Gout Flares:**  
• Administer a single dose of colchicine 0.6 mg, followed by colchicine 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 twice daily, decrease to colchicine 0.3 mg once daily. If dose 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 twice daily. |
|  | EVG/c | ↑ colchicine expected |  |
| **Dronabinol** | BIC, DTG, RAL | ↔ dronabinol expected | No dose adjustment needed.  
Monitor for dronabinol-related adverse events. |
<p>|  | EVG/c | ↑ dronabinol possible |  |</p>
<table>
<thead>
<tr>
<th>Concomitant Drug</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>Eluxadoline</strong></td>
<td>BIC, DTG, RAL</td>
<td>↔ eluxadoline expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ eluxadoline possible</td>
<td>Monitor for eluxadoline-related adverse events.</td>
<td></td>
</tr>
<tr>
<td><strong>Ergot Derivatives</strong></td>
<td>BIC, DTG, RAL</td>
<td>↔ dihydroergotamine, ergotamine, and methylergonovine expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ dihydroergotamine, ergotamine, and methylergonovine expected</td>
<td>Contraindicated.</td>
<td></td>
</tr>
<tr>
<td><strong>Flibanserin</strong></td>
<td>BIC, DTG, RAL</td>
<td>↔ flibanserin expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ flibanserin expected</td>
<td>Contraindicated.</td>
<td></td>
</tr>
<tr>
<td><strong>Polyvalent Cation Supplements</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mg, Al, Fe, Ca, Zn, including multivitamins with minerals</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Note:</strong> Please refer to the Acid Reducers section in this table for recommendations on use with Al-, Mg-, and Ca-containing antacids.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>BIC</strong></td>
<td></td>
<td>↔ BIC AUC if administered simultaneously with Fe or Ca and food</td>
<td>With Supplements That Contain Ca or Fe:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BIC AUC ↓ 33% if administered simultaneously with CaCO₃ under fasting conditions</td>
<td>• Administer BIC and supplements that contain Ca or Fe together with food.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BIC AUC ↓ 63% if administered simultaneously with Fe under fasting conditions</td>
<td>Do not coadminister BIC under fasting conditions simultaneously with, or 2 hours after, supplements that contain Ca or Fe.</td>
</tr>
<tr>
<td><strong>DTG</strong></td>
<td></td>
<td>DTG AUC ↓ 39% if administered simultaneously with CaCO₃ under fasting conditions</td>
<td>With Supplements That Contain Ca or Fe:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DTG AUC ↓ 54% if administered simultaneously with Fe under fasting conditions</td>
<td>• Administer DTG and supplements that contain Ca or Fe together with food, or administer DTG at least 2 hours before or at least 6 hours after supplement.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↔ DTG when administered with Ca or Fe supplement simultaneously with food</td>
<td>Do not coadminister DTG under fasting conditions simultaneously with, or 2 hours after, supplements that contain Ca or Fe.</td>
</tr>
<tr>
<td><strong>EVG/c, RAL</strong></td>
<td></td>
<td>↓ INSTI possible</td>
<td>If coadministration is necessary, administer INSTI at least 2 hours before or at least 6 hours after supplements that contain polyvalent cations, including but not limited to the following products: cation-containing laxatives; Fe, Ca, or Mg supplements; and sucralfate. Monitor for virologic response.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Many oral multivitamins also contain varying amounts of polyvalent cations; the extent and significance of chelation is unknown.</td>
<td></td>
</tr>
</tbody>
</table>

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

**Key:** Al = aluminum; ART = antiretroviral therapy; ARV = antiretroviral; AUC = area under the curve; BIC = bictegravir; Ca = calcium; CaCO₃ = calcium carbonate; CCB = calcium channel blocker; C max = maximum plasma concentration; C min = minimum plasma concentration; COBI = cobicistat; CrCl = creatinine clearance; CYP = cytochrome P; DAA = direct-acting antiviral; DTG = dolutegravir; ECG = electrocardiogram; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; Fe = iron; FTC = emtricitabine; HCV = hepatitis C virus; INR= international normalized ratio; INSTI = integrase strand transfer inhibitor; Mg = magnesium; PAH = pulmonary arterial hypertension; PDE5 = Phosphodiesterase Type 5; PTH = parathyroid hormone; RAL = raltegravir; RTV = ritonavir; SSRI = selective serotonin reuptake inhibitors; TAF = tenofovir alafenamide; TCA = tricyclic antidepressants; TDF = tenofovir disoproxil fumarate; Zn = zinc

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

Downloaded from https://aidsinfo.nih.gov/guidelines on 7/3/2020
In the table below, “No dose adjustment needed” indicates that the FDA-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 drug is being initiated in a patient on a stable concomitant medication or 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. In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgement to select the most appropriate alternative medication to use.

<table>
<thead>
<tr>
<th>Concomitant Drug Class/Name</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>Antibacterial Agents</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Antimycobacterials</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rifabutin</td>
<td>↓ MVC possible</td>
<td>If Used Without a Strong CYP3A Inhibitor:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• MVC 300 mg twice daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td>If Used With a Strong CYP3A Inhibitor:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• MVC 150 mg twice daily</td>
</tr>
<tr>
<td>Rifampin</td>
<td>MVC AUC ↓ 63%</td>
<td>If Used Without a Strong CYP3A Inhibitor:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• MVC 600 mg twice daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td>If Used With a Strong CYP3A Inhibitor:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Consider alternative ARV or antimalarial</td>
</tr>
<tr>
<td>Rifapentine</td>
<td>↓ MVC expected</td>
<td>Do not coadminister</td>
</tr>
<tr>
<td><strong>Macrolides</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azithromycin</td>
<td>↔ MVC expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>↑ MVC possible</td>
<td>MVC 150 mg twice daily</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>↑ MVC possible</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td><strong>Anticonvulsants</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbamazepine, Phenobarbital, Phenytoin</td>
<td>↓ MVC possible</td>
<td>If Used Without a Strong CYP3A Inhibitor:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• MVC 600 mg twice daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td>If Used With a Strong CYP3A Inhibitor:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• MVC 150 mg twice daily</td>
</tr>
<tr>
<td>Eslicarbazepine</td>
<td>↓ MVC possible</td>
<td>Consider alternative ARV or anticonvulsant.</td>
</tr>
<tr>
<td>Oxcarbazepine</td>
<td>↓ MVC possible</td>
<td>Consider alternative ARV or anticonvulsant.</td>
</tr>
<tr>
<td><strong>Antifungals</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluconazole</td>
<td>↑ MVC possible</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>Isavuconazole</td>
<td>↑ MVC possible</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>Itraconazole</td>
<td>↑ MVC possible</td>
<td>MVC 150 mg twice daily</td>
</tr>
<tr>
<td>Posaconazole</td>
<td>↑ MVC possible</td>
<td>MVC 150 mg twice daily</td>
</tr>
<tr>
<td>Voriconazole</td>
<td>↑ MVC possible</td>
<td>MVC 150 mg twice daily</td>
</tr>
<tr>
<td><strong>Hepatitis C Direct-Acting Antivirals</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daclatasvir</td>
<td>↔ MVC expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>↔ daclatasvir expected</td>
<td></td>
</tr>
<tr>
<td>Dasabuvir plus Ombitasvir/ Paritaprevir/RTV</td>
<td>↑ MVC expected</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elbasvir/Grazoprevir</td>
<td>↔ MVC expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>Concomitant Drug Class/Name</td>
<td>Effect on CCR5 Antagonist and/or Concomitant Drug Concentrations</td>
<td>Dosing Recommendations and Clinical Comments</td>
</tr>
<tr>
<td>----------------------------</td>
<td>---------------------------------------------------------------</td>
<td>---------------------------------------------</td>
</tr>
<tr>
<td><strong>Hepatitis C Direct-Acting Antivirals</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glecaprevir/Pibrentasvir</td>
<td>↔ MVC expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>Ledipasvir/Sofosbuvir</td>
<td>↔ MVC expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>Simeprevir</td>
<td>↔ MVC expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>Sofosbuvir</td>
<td>↔ MVC expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>Sofosbuvir/Velpatasvir</td>
<td>↔ MVC expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>Sofosbuvir/Velpatasvir/Voxilaprevir</td>
<td>↔ MVC expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td><strong>Herbal Products</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>St. John's Wort</td>
<td>↓ MVC expected</td>
<td>Do not coadminister.</td>
</tr>
<tr>
<td><strong>Hormonal Therapies</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>St. John's Wort</td>
<td>↓ ethinyl estradiol or levonorgestrel</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td><strong>Menopausal Hormone Replacement Therapy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>St. John's Wort</td>
<td>↑ MVC or hormone replacement therapies expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td><strong>Gender-Affirming Hormone Therapies</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>St. John's Wort</td>
<td>↔ MVC or gender-affirming hormones expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td><strong>Antiretroviral Drugs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>INSTIs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BIC, DTG</td>
<td>↔ MVC expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EVG/c</td>
<td>↑ MVC possible</td>
<td>MVC 150 mg twice daily</td>
</tr>
<tr>
<td>RAL</td>
<td>MVC AUC ↓ 21%</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>RAL AUC ↓ 37%</td>
<td></td>
</tr>
<tr>
<td><strong>NNRTIs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOR, RPV</td>
<td>↔ MVC expected</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>EFV</td>
<td>MVC AUC ↓ 45%</td>
<td><strong>If Used Without a Strong CYP3A Inhibitor:</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• MVC 600 mg twice daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>If Used With a Strong CYP3A Inhibitor:</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• MVC 150 mg twice daily</td>
</tr>
<tr>
<td>ETR</td>
<td>MVC AUC ↓ 53%</td>
<td><strong>If Used Without a Strong CYP3A Inhibitor:</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• MVC 600 mg twice daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>If Used With a Strong CYP3A Inhibitor:</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• MVC 150 mg twice daily</td>
</tr>
<tr>
<td>NVP</td>
<td>↔ MVC AUC</td>
<td><strong>If Used Without a Strong CYP3A Inhibitor:</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• MVC 300 mg twice daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>If Used With a Strong CYP3A Inhibitor:</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• MVC 150 mg twice daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• With TPV/r, use MVC 300 mg twice daily</td>
</tr>
<tr>
<td><strong>PIs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATV, ATV/c, ATV/r</td>
<td>With Unboosted ATV:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• MVC AUC ↑ 257%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>With (ATV/r 300 mg/100 mg) Once Daily:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• MVC AUC ↑ 388%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>MVC 150 mg twice daily</td>
<td></td>
</tr>
</tbody>
</table>
Table 21e. Drug Interactions between the CCR5 Antagonist Maraviroc and Other Drugs (Including Antiretroviral Agents)  *(Last updated December 18, 2019; last reviewed December 18, 2019)*  (page 3 of 3)

<table>
<thead>
<tr>
<th>Concomitant Drug Class/Name</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>
</tr>
<tr>
<td><strong>DRV/c, DRV/r</strong></td>
<td>With (DRV/r 600 mg/100 mg) Twice Daily:</td>
<td>MVC 150 mg twice daily</td>
</tr>
<tr>
<td></td>
<td>• MVC AUC ↑ 305%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>With (DRV/r 600 mg/100 mg) Twice Daily and ETR:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• MVC AUC ↑ 210%</td>
<td></td>
</tr>
<tr>
<td><strong>LPV/r</strong></td>
<td>MVC AUC ↑ 295%</td>
<td>MVC 150 mg twice daily</td>
</tr>
<tr>
<td></td>
<td>With LPV/r and EFV:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• MVC AUC ↑ 153%</td>
<td></td>
</tr>
<tr>
<td><strong>TPV/r</strong></td>
<td>With (TPV/r 500 mg/200 mg) Twice Daily:</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>• ↔ MVC AUC</td>
<td></td>
</tr>
</tbody>
</table>

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

**Key:** ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; CYP = cytochrome P; DOR = doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FDA = Food and Drug Administration; INSTI = integrase strand transfer inhibitor; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; TPV/r = tipranavir/ritonavir
### Table 22a. Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 1 of 2)

**Note:** Interactions associated with DLV, FPV, IDV, NFV, and SQV are not included in this table. Please refer to the FDA product labels for information regarding interactions between these drugs and other concomitant drugs.

<table>
<thead>
<tr>
<th>PI(s)</th>
<th>Drug(s)</th>
<th>NNRTIs</th>
<th>PK Data Type</th>
<th>Dose</th>
<th>ATV Unboosted</th>
<th>ATV/c</th>
<th>DRV/c</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>DOR</td>
<td>ETR</td>
<td>NVP</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>↔ DOR expected</td>
<td>↑ ETR AUC</td>
<td>↑ NVP possible</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>↔ EFV</td>
<td>↓ ATV AUC</td>
<td>↔ ATV expected</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>↓ COBI possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Do not administer.</td>
<td>Do not administer.</td>
<td>Do not administer.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No dose adjustment needed.</td>
<td>No dose adjustment needed.</td>
<td>No dose adjustment needed.</td>
</tr>
</tbody>
</table>

#### ATV

**PK Data**

- ↑ DOR expected
- ↔ ATV expected

**Efavirenz (EFV)**

- ↔ EFV expected
- ↓ ATV possible
- ↓ COBI possible

**Entecavir (ETR)**

- ↑ ETR possible
- ↓ ATV possible
- ↓ COBI possible

**Nevirapine (NVP)**

- ↑ NVP possible
- ↓ ATV possible

**Ritonavir (RPV)**

- ↑ RPV possible
- ↔ ATV expected

**Dose**

- No dose adjustment needed.

**ATV/c**

**PK Data**

- ↑ DOR expected
- ↔ ATV expected

**Efavirenz (EFV)**

- ↔ EFV expected
- ↓ ATV possible
- ↓ COBI possible

**Entecavir (ETR)**

- ↑ ETR possible
- ↓ ATV possible
- ↓ COBI possible

**Nevirapine (NVP)**

- ↑ NVP possible
- ↓ ATV possible
- ↓ COBI possible

**Ritonavir (RPV)**

- ↑ RPV possible
- ↔ ATV expected

**Dose**

- No dose adjustment needed.

**ATV/r**

- ↑ DOR expected
- ↔ ATV expected

**Efavirenz (EFV)**

- ↔ EFV expected
- ↓ DRV possible
- ↓ COBI possible

**Entecavir (ETR)**

- ↔ ETR AUC and C_{min}
- ↔ DRV AUC and C_{min}
- ↓ 56%
- COBI AUC ↓ 30% and C_{min} ↓ 66%

**Nevirapine (NVP)**

- ↑ NVP possible
- ↓ DRV possible
- ↓ COBI possible

**Ritonavir (RPV)**

- ↑ RPV possible
- ↔ ATV expected

**Dose**

- No dose adjustment needed.

**DRV/c**

- ↑ DOR expected
- ↔ DRV expected

**Efavirenz (EFV)**

- ↔ EFV expected
- ↓ DRV possible
- ↓ COBI possible

**Entecavir (ETR)**

- ↔ ETR AUC and C_{min}
- ↔ DRV AUC and C_{min}
- ↓ 56%
- COBI AUC ↓ 30% and C_{min} ↓ 66%

**Nevirapine (NVP)**

- ↑ NVP possible
- ↓ DRV possible
- ↓ COBI possible

**Ritonavir (RPV)**

- ↔ DRV expected
- ↑ RPV possible

**Dose**

- No dose adjustment needed.

**ATV**

- No dose adjustment needed.

**ATV/r**

- No dose adjustment needed.

**DRV/c**

- No dose adjustment needed.
<table>
<thead>
<tr>
<th>NNRTIs</th>
<th>DOR</th>
<th>EFV</th>
<th>ETR</th>
<th>NVP</th>
<th>RPV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DRV/r</strong></td>
<td>PK Data</td>
<td>Data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PI</td>
<td>↓ DOR expected ↔ DRV expected</td>
<td>With (DRV 300 mg plus RTV 100 mg) Twice Daily:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• EFV AUC ↑ 21%</td>
<td>• ↔ DRV AUC and C&lt;sub&gt;min&lt;/sub&gt; ↓ 31%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ETR 100 mg Twice Daily with (DRV 600 mg plus RTV 100 mg) Twice Daily:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• ETR AUC ↓ 37% and C&lt;sub&gt;min&lt;/sub&gt; ↓ 49%</td>
<td>• ↔ DRV</td>
<td>With (DRV 400 mg plus RTV 100 mg) Twice Daily:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• NVP AUC ↑ 27% and C&lt;sub&gt;min&lt;/sub&gt; ↑ 47%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• DRV AUC ↑ 24%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>LPV/r</strong></td>
<td>PK Data</td>
<td>Data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PI</td>
<td>↑ DOR expected ↔ LPV expected</td>
<td>With LPV/r 500 mg/125 mg&lt;sup&gt;a&lt;/sup&gt; Twice Daily:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• LPV concentration similar to that of LPV/r 400 mg/100 mg twice daily without EFV</td>
<td>• ↔ EFV expected</td>
<td>ETR AUC ↓ 35% (comparable to the decrease seen with DRV/r)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>↔ LPV AUC</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dose</td>
<td>No dose adjustment needed.</td>
<td>No dose adjustment needed.</td>
<td>No dose adjustment needed.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Data</td>
<td>LPV/r 500 mg/125 mg&lt;sup&gt;b&lt;/sup&gt; twice daily</td>
<td>LPV/r 533 mg/133 mg twice daily when using oral solution</td>
<td>No dose adjustment needed for EFV.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>No dose adjustment needed for LPV.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TPV/r</strong></td>
<td>PK Data</td>
<td>Data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PI</td>
<td>↑ DOR expected ↔ TPV expected</td>
<td>With (TPV 500 mg plus RTV 100 mg) Twice Daily:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• ↔ EFV</td>
<td>• TPV AUC ↓ 31% and C&lt;sub&gt;min&lt;/sub&gt; ↓ 42%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>With (TPV 750 mg plus RTV 200 mg) Twice Daily:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• ↔ EFV and TPV</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dose</td>
<td>No dose adjustment needed.</td>
<td>No dose adjustment needed.</td>
<td>Do not coadminister.</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td></td>
<td>Data</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> DRV concentration was compared to a historic control.

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

**Key to Symbols:**

<table>
<thead>
<tr>
<th>↑</th>
<th>↓</th>
<th>↔</th>
</tr>
</thead>
<tbody>
<tr>
<td>increase</td>
<td>decrease</td>
<td>no change</td>
</tr>
</tbody>
</table>

**Key:**

- ART = antiretroviral therapy; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; C<sub>min</sub> = minimum plasma concentration; COBI = cobicistat; DLV = delavirdine; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; EFV = efavirenz; ETR = etravirine; FDA = Food and Drug Administration; FPV = fosamprenavir; IDV = indinavir; LPV = lopinavir; LPV/r = lopinavir/ritonavir; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PK = pharmacokinetic; RPV = rilpivirine; RTV = ritonavir; SQV = saquinavir; TPV = tipranavir; TPV/r = tipranavir/ritonavir
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 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 22b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors  *(Last updated December 18, 2019; last reviewed December 18, 2019)*

<table>
<thead>
<tr>
<th>ARV Drugs by Drug Class</th>
<th>INSTIs</th>
<th>BIC</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>
<td></td>
</tr>
<tr>
<td>DOR</td>
<td>PK Data</td>
<td>↔ DOR and BIC expected</td>
<td>↔ DOR</td>
<td>↑ DOR expected</td>
<td>↔ DOR and RAL expected</td>
</tr>
<tr>
<td></td>
<td>Dose</td>
<td>No dose adjustment needed</td>
<td>No dose adjustment needed</td>
<td>No dose adjustment needed</td>
<td>No dose adjustment needed</td>
</tr>
<tr>
<td>EFV</td>
<td>PK Data</td>
<td>↓ BIC expected</td>
<td>With DTG 50 mg Once Daily: • DTG AUC ↓ 57% and C_{min} ↓ 75%</td>
<td>↑ or ↓ EVG, COBI, and EFV possible</td>
<td>With RAL 400 mg Twice Daily: • RAL AUC ↓ 36% and C_{min} ↓ 21%</td>
</tr>
<tr>
<td></td>
<td>Dose</td>
<td>Do not coadminister.</td>
<td>In Patients Without INSTI Resistance: • DTG 50 mg twice daily</td>
<td>Do not coadminister.</td>
<td>With RAL 1,200 mg Once Daily: • ↔ RAL AUC and C_{min}</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ETR</td>
<td>PK Data</td>
<td>↓ BIC expected</td>
<td>ETR 200 mg Twice Daily plus DTG 50 mg Once Daily: • DTG AUC ↓ 71% and C_{min} ↓ 88%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Data* indicates that the concurrent administration of the drugs is not recommended.

*ARV* indicates antiretroviral.

*INSTIs* indicate integrase strand transfer inhibitors.

*NNRTIs* indicate non-nucleoside reverse transcriptase inhibitors.

*PK* indicates pharmacokinetic.

*RTV* indicates ritonavir.

*DRV* indicates darunavir.

*LPI* indicates lopinavir.

*DTG* indicates dolutegravir.

*RAL* indicates raltegravir.

*EFV* indicates efavirenz.

*COBI* indicates cobicistat.

*ETR* indicates etravirine.

*a* Indicates resistance to INSTI or certain INSTI-associated resistance.

---

*Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV* 117

Downloaded from [https://aidsinfo.nih.gov/guidelines](https://aidsinfo.nih.gov/guidelines) on 7/3/2020
Table 22b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors  

**ARV Drugs by Drug Class**

<table>
<thead>
<tr>
<th>ARV Drugs by Drug Class</th>
<th>INSTIs</th>
<th>BIC</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>
<td></td>
</tr>
<tr>
<td>ETR</td>
<td>Dose</td>
<td>Do not coadminister.</td>
<td>Do not coadminister ETR and DTG without concurrently administering ATV/r, DRV/r, or LPV/r.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>PK Data</td>
<td>‡ BIC expected</td>
<td>With DTG 50 mg Once Daily:</td>
<td>† or ↓ EVG, COBI, and NVP possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• DTG AUC ↓ 19% and C_{min} ↓ 34%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>In Patients Without INSTI Resistance:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• DTG 50 mg once daily with ETR (concurrently with ATV/r, DRV/r, or LPV/r)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>In Patients With Certain INSTI-Associated Resistance* or Clinically Suspected INSTI Resistance:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• DTG 50 mg twice daily with ETR (concurrently with ATV/r, DRV/r, or LPV/r)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dose</td>
<td>No dose adjustment needed.</td>
<td>No dose adjustment needed.</td>
<td>Do not coadminister.</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>NVP</td>
<td>PK Data</td>
<td>No data</td>
<td>With DTG 50 mg Once Daily:</td>
<td>† or ↓ EVG, COBI, and RPV possible</td>
<td>↔ RPV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• ↔ DTG AUC and C_{min} ↑ 22%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• ↔ RPV AUC and C_{min} ↑ 21%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>No data</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PIs</td>
<td>PK Data</td>
<td>No data</td>
<td>ATV 400 mg Once Daily plus BIC 75 mg Single Dose:</td>
<td>No data</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>BIC AUC ↑ 315%</td>
<td>(ATV 400 mg plus DTG 30 mg) Once Daily:</td>
<td>No data</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• DTG AUC ↑ 91% and C_{min} ↑ 180%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dose</td>
<td>Do not coadminister.</td>
<td>No dose adjustment needed.</td>
<td>Do not coadminister.</td>
<td>No dose adjustment needed.</td>
</tr>
<tr>
<td>ATV/c</td>
<td>PK Data</td>
<td>BIC AUC ↑ 306%</td>
<td>No data</td>
<td>Not applicable</td>
<td>No data</td>
</tr>
<tr>
<td></td>
<td>Dose</td>
<td>Do not coadminister.</td>
<td>No dose adjustment needed.</td>
<td>Do not coadminister two COBI-containing products.</td>
<td>No dose adjustment needed.</td>
</tr>
</tbody>
</table>
### Table 22b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors  
(Last updated December 18, 2019; last reviewed December 18, 2019)  
(continued)

<table>
<thead>
<tr>
<th>ARV Drugs by Drug Class</th>
<th>INSTIs</th>
<th>BIC</th>
<th>DTG</th>
<th>EVG/c</th>
<th>RAL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ATV/r</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PK Data</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose</td>
<td>Do not coadminister.</td>
<td>No dose adjustment needed.</td>
<td>Do not coadminister RTV and COBI.</td>
<td>No dose adjustment needed.</td>
<td></td>
</tr>
<tr>
<td><strong>DRV</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PK Data</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td>↔ DRV or EVG expected</td>
<td>Not applicable</td>
<td></td>
</tr>
<tr>
<td>Dose</td>
<td>Do not administer DRV without RTV or COBI</td>
<td>Do not administer DRV without RTV or COBI</td>
<td>No dose adjustment needed.</td>
<td>Do not administer DRV without RTV or COBI.</td>
<td></td>
</tr>
<tr>
<td><strong>DRV/c</strong></td>
<td>PK Data</td>
<td>BIC AUC ↑ 74%</td>
<td>DRV/c plus DTG Once Daily:</td>
<td>Not applicable</td>
<td>No data</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• ↔ DTG, DRV, and COBI</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>DTG 50 mg Once Daily and DRV/r Once Daily Switched to DRV/c:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• DTG C&lt;sub&gt;min&lt;/sub&gt; ↑ 100%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose</td>
<td>No dose adjustment needed.</td>
<td>No dose adjustment needed.</td>
<td>Do not coadminister two COBI-containing products.</td>
<td>No dose adjustment needed.</td>
<td></td>
</tr>
<tr>
<td><strong>DRV/r</strong></td>
<td>PK Data</td>
<td>No data</td>
<td>(DRV 600 mg plus RTV 100 mg) Twice Daily with DTG 30 mg Once Daily:</td>
<td>Not applicable</td>
<td>No data</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• ↔ DTG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose</td>
<td>No dose adjustment needed.</td>
<td>No dose adjustment needed.</td>
<td>Do not coadminister RTV and COBI.</td>
<td>No dose adjustment needed.</td>
<td></td>
</tr>
<tr>
<td><strong>LPV/r</strong></td>
<td>PK Data</td>
<td>No data</td>
<td>With (LPV 400 mg plus RTV 100 mg) Twice Daily and DTG 30 mg Once Daily:</td>
<td>Not applicable</td>
<td>↓ RAL ↔ LPV/r</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• ↔ DTG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose</td>
<td>Consider alternative combination.</td>
<td>No dose adjustment needed.</td>
<td>Do not coadminister RTV and COBI.</td>
<td>No dose adjustment needed.</td>
<td></td>
</tr>
<tr>
<td><strong>TPV/r</strong></td>
<td>PK Data</td>
<td>↓ BIC possible</td>
<td>With (TPV 500 mg plus RTV 200 mg) Twice Daily and DTG 50 mg Once Daily:</td>
<td>Not applicable</td>
<td>With (TPV 500 mg plus RTV 200 mg) Twice Daily and RAL 400 mg Twice Daily:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• DTG AUC ↓ 59% and C&lt;sub&gt;min&lt;/sub&gt; ↓ 76%</td>
<td></td>
<td>• RAL AUC ↓ 24% and C&lt;sub&gt;min&lt;/sub&gt; ↓ 55%</td>
</tr>
</tbody>
</table>
### Table 22b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors  
(Last updated December 18, 2019; last reviewed December 18, 2019)  (page 4 of 4)

<table>
<thead>
<tr>
<th>ARV Drugs by Drug Class</th>
<th>INSTIs</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BIC</td>
<td>DTG</td>
<td>EVG/c</td>
</tr>
<tr>
<td><strong>TPV/r</strong></td>
<td>Do not coadminister.</td>
<td>In Patients Without INSTI Resistance: • DTG 50 mg twice daily</td>
<td>Do not coadminister RTV and COBI.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>In Patients With Certain INSTI-Associated Resistance or Clinically Suspected INSTI Resistance: • Consider alternative combination.</td>
<td></td>
</tr>
</tbody>
</table>

* Refer to DTG product label for details.

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

**Key:** ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; C<sub>min</sub> = minimum plasma concentration; COBI = cobicistat; CYP = cytochrome P; DOR = doravirine; 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. Coformulated Single-Tablet Regimens

The following table includes dose recommendations for FDA-approved STR products. Please see the class-specific drug characteristics tables (Appendix B, Tables 3 to 6) for details about the individual drugs included in these STR products, including information on elimination and metabolic pathways, serum and intracellular half-lives, and adverse effects. The STR products in this table are listed by drug class and arranged in alphabetical order by trade name within each class.

<table>
<thead>
<tr>
<th>Trade Name (Abbreviations)</th>
<th>ARV Drugs Included in the STR</th>
<th>Dosing Recommendationa</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>INSTI plus Two NRTIs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biktarvy (BIC/TAF/FTC)</td>
<td>Bictegravir 50 mg/tenofovir alafenamide 25 mg/emtricitabine 200 mg</td>
<td>One tablet once daily</td>
</tr>
<tr>
<td>Genvoya (EVG/c/TAF/FTC)</td>
<td>Elvitegravir 150 mg/cobicistat 150 mg/tenofovir alafenamide 10 mg/emtricitabine 200 mg</td>
<td>One tablet once daily with food</td>
</tr>
<tr>
<td>Stribild (EVG/c/TDF/FTC)</td>
<td>Elvitegravir 150 mg/cobicistat 150 mg/tenofovir disoproxil fumarate 300 mg/emtricitabine 200 mg</td>
<td>One tablet once daily with food</td>
</tr>
<tr>
<td>Triumeq (DTG/ABC/3TC)</td>
<td>Dolutegravir 50 mg/abacavir 600 mg/lamivudine 300 mg</td>
<td>One tablet once daily</td>
</tr>
<tr>
<td><strong>INSTI plus One NRTI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dovato (DTG/3TC)</td>
<td>Dolutegravir 50 mg/lamivudine 300 mg</td>
<td>One tablet once daily</td>
</tr>
<tr>
<td><strong>PI plus Two NRTIs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symtuza (DRV/c/TAF/FTC)</td>
<td>Darunavir 800 mg/cobicistat 150 mg/tenofovir alafenamide 10 mg/emtricitabine 200 mg</td>
<td>One tablet once daily with food</td>
</tr>
<tr>
<td><strong>NNRTI plus Two NRTIs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atripla (EFV/TDF/FTC)</td>
<td>Efavirenz 600 mg/tenofovir disoproxil fumarate 300 mg/emtricitabine 200 mg</td>
<td>One tablet once daily on an empty stomach, preferably at bedtime</td>
</tr>
<tr>
<td>Complera (RPV/TDF/FTC)</td>
<td>Rilpivirine 25 mg/tenofovir disoproxil fumarate 300 mg/emtricitabine 200 mg</td>
<td>One tablet once daily with a meal</td>
</tr>
<tr>
<td>Delstrigo (DOR/TDF/3TC)</td>
<td>Doravirine 100 mg/tenofovir disoproxil fumarate 300 mg/lamivudine 300 mg</td>
<td>One tablet once daily</td>
</tr>
<tr>
<td>Odefsey (RPV/ITAF/FTC)</td>
<td>Rilpivirine 25 mg/tenofovir alafenamide 25 mg/emtricitabine 200 mg</td>
<td>One tablet once daily with a meal</td>
</tr>
<tr>
<td>Symfi (EFV/TDF/3TC)</td>
<td>Efavirenz 600 mg/tenofovir disoproxil fumarate 300 mg/lamivudine 300 mg</td>
<td>One tablet once daily on an empty stomach, preferably at bedtime</td>
</tr>
<tr>
<td>Symfi Lo (EFV/TDF/3TC)</td>
<td>Efavirenz 400 mg/tenofovir disoproxil fumarate 300 mg/lamivudine 300 mg</td>
<td>One tablet once daily on an empty stomach, preferably at bedtime</td>
</tr>
<tr>
<td><strong>INSTI plus One NNRTI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Juluca (DTG/RPV)</td>
<td>Dolutegravir 50 mg/ritampirine 25 mg</td>
<td>One tablet once daily with a meal</td>
</tr>
</tbody>
</table>

a For dose adjustments in patients with renal or hepatic insufficiency, see Appendix B, Table 10. When no food restriction is listed, the STR can be taken with or without food.

**Key:**
- 3TC = lamivudine
- ABC = abacavir
- ARV = antiretroviral
- BIC = bictegravir
- DOR = doravirine
- DRV = darunavir
- DRV/c = darunavir/cobicistat
- DTG = dolutegravir
- EFV = efavirenz
- EVG = elvitegravir
- FTC = emtricitabine
- INSTI = integrase strand transfer inhibitor
- NNRTI = non-nucleoside reverse transcriptase inhibitor
- NRTI = nucleoside reverse transcriptase inhibitor
- PI = protease inhibitor
- RPV = rilpivirine
- STR = single-tablet regimen
- TAF = tenofovir alafenamide
- TDF = tenofovir disoproxil fumarate

*Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV*
Appendix B, Table 2. Nucleoside Reverse Transcriptase Inhibitor-Based, Fixed-Dose Combination Tablets for Use as Part of an Antiretroviral Regimen  (Last updated July 10, 2019; last reviewed December 18, 2019)

The following table includes dose recommendations for FDA-approved, dual-NRTI FDC products. These FDC tablets are not complete regimens and must be administered in combination with other ARV drugs.

Please see the class-specific drug characteristics tables (Appendix B, Tables 3 to 6) for details about the individual drugs contained in these FDC products, including information on elimination and metabolic pathways, serum and intracellular half-lives, and adverse effects. The FDC tablets in this table are listed by trade name.

<table>
<thead>
<tr>
<th>Trade Name (Abbreviations)</th>
<th>ARV Drugs Included in the FDC Tablet</th>
<th>Dosing Recommendation*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TAF or TDF plus an NRTI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Descovy (TAF/FTC)</td>
<td>Tenofovir alafenamide 25 mg/emtricitabine 200 mg</td>
<td>One tablet once daily</td>
</tr>
<tr>
<td>Cimduo (TDF/3TC)</td>
<td>Tenofovir disoproxil fumarate 300 mg/lamivudine 300 mg</td>
<td>One tablet once daily</td>
</tr>
<tr>
<td>Temixys (TDF/3TC)</td>
<td>Tenofovir disoproxil fumarate 300 mg/lamivudine 300 mg</td>
<td>One tablet once daily</td>
</tr>
<tr>
<td>Truvada (TDF/FTC)</td>
<td>Tenofovir disoproxil fumarate 300 mg/emtricitabine 200 mg</td>
<td>One tablet once daily</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Other NRTI-Based, FDC Tablets</strong></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Epzicom (ABC/3TC)</td>
<td>Abacavir 600 mg/lamivudine 300 mg</td>
<td>One tablet once daily</td>
</tr>
<tr>
<td><strong>Note:</strong> Generic product is available.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combivir (ZDV/3TC)</td>
<td>Zidovudine 300 mg/lamivudine 150 mg</td>
<td>One tablet twice daily</td>
</tr>
<tr>
<td><strong>Note:</strong> Generic product is available.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* For dose adjustments in patients with renal or hepatic insufficiency, see Appendix B, Table 10. All FDC tablets listed in this table can be taken without regard to food.

Key: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; FDA = Food and Drug Administration; FDC = fixed-dose combination; FTC = emtricitabine; NRTI = nucleoside reverse transcriptase inhibitor; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; ZDV = zidovudine
Appendix B, Table 3. Characteristics of Nucleoside Reverse Transcriptase Inhibitors *(Last updated December 18, 2019; last reviewed December 18, 2019)* (page 1 of 4)

The older NRTIs ddI and d4T are no longer commonly used in clinical practice and have been removed from this table. Please refer to the July 10, 2019, version of the guidelines (found in the archived guidelines section of AIDSinfo) or to the FDA product labels for ddI and d4T for information regarding these drugs.

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation)</th>
<th>Formulations</th>
<th>Dosing Recommendations</th>
<th>Elimination/Metabolic Pathway</th>
<th>Serum/Intracellular Half-Lives</th>
<th>Adverse Events</th>
</tr>
</thead>
</table>
| **Abacavir (ABC) Ziagen** | **Ziagen:** 300 mg tablet  
20 mg/mL oral solution | **Ziagen:**  
ABC 600 mg once daily, or  
ABC 300 mg twice daily  
See Appendix B, Tables 1 and 2 for dosing information for FDC tablets that contain ABC. | Metabolized by alcohol dehydrogenase and glucuronyl transferase  
82% of ABC dose is excreted renally as metabolites  
Dose adjustment is recommended in patients with hepatic insufficiency (see Appendix B, Table 10). | 1.5 hours/12–26 hours | Patients who test positive for HLA-B*5701 are at the highest risk of experiencing HSRs. HLA screening should be done before initiating ABC.  
For patients with a history of HSRs, rechallenge is not recommended.  
Symptoms of HSRs may include fever, rash, nausea, vomiting, diarrhea, abdominal pain, malaise, fatigue, or respiratory symptoms (e.g., sore throat, cough, or shortness of breath).  
Some cohort studies suggest an increased risk of MI with recent or current use of ABC, but this risk is not substantiated in other studies. |
| **Note:** Generic tablet formulation is available. |  
**Generic:** 300 mg tablet  
Also available as FDC with 3TC and ZDV/3TC  
**FDC Tablets that Contain ABC:**  
Epzicom (ABC/3TC)  
Trizivir (ABC/ZDV/3TC)  
**STRs that Contain ABC:**  
Triumeq (DTG/ABC/3TC) |  
Emtriva Capsule:  
FTC 200 mg once daily  
Oral Solution:  
FTC 240 mg (24 mL) once daily  
See Appendix B, Tables 1 and 2 for dosing information for FDC tablets that contain FTC. | 86% of FTC dose is excreted renally  
See Appendix B, Table 10 for dosing recommendations in patients with renal insufficiency. | 10 hours/>20 hours | Minimal toxicity  
Hyperpigmentation/skin discoloration  
Severe acute exacerbation of hepatitis may occur in patients with HBV/AIDS coinfection who discontinue FTC. |
| **Emtricitabine (FTC) Emtriva** | **Emtriva:**  
200 mg hard gelatin capsule  
10 mg/mL oral solution  
**FDC Tablets that Contain FTC:**  
Descovy (TAF/FTC)  
Truvada (TDF/FTC)  
**STRs that Contain FTC:**  
Atripla (EFV/TDF/FTC)  
Biktarvy (BIC/TAF/FTC)  
Complera (RPV/TDF/FTC)  
Genvoya (EVI/c/TAF/FTC)  
Odefsey (RPV/TAF/FTC)  
Stribild (EVG/c/TDF/FTC)  
Symtuza (DRV/c/TAF/FTC) |  
Emtriva Capsule:  
FTC 200 mg once daily  
Oral Solution:  
FTC 240 mg (24 mL) once daily  
See Appendix B, Tables 1 and 2 for dosing information for FDC tablets that contain FTC. | |  | |
### Appendix B, Table 3. Characteristics of Nucleoside Reverse Transcriptase Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 2 of 4)

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation)</th>
<th>Formulations</th>
<th>Dosing Recommendations</th>
<th>Elimination/ Metabolic Pathway</th>
<th>Serum/ Intracellular Half-Lives</th>
<th>Adverse Events&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lamivudine</strong> (3TC) <em>Epivir</em>&lt;br&gt;Note: Generic products are available.</td>
<td>Epivir: • 150 and 300 mg tablets • 10 mg/mL oral solution&lt;br&gt;Generic: • 150 and 300 mg tablets • Also available as FDC with ABC and ZDV&lt;br&gt;FDC Tablets that Contain 3TC:&lt;br&gt;• Cimduo (TDF/3TC)&lt;br&gt;• Combivir (ZDV/3TC)&lt;br&gt;• Epzicom (ABC/3TC)&lt;br&gt;• Temixys (TDF/3TC)&lt;br&gt;• Trizivir (ABC/ZDV/3TC)&lt;br&gt;STRs that Contain 3TC:&lt;br&gt;• Delstrigo (DOR/TDF/3TC)&lt;br&gt;• Dovato (DTG/3TC)&lt;br&gt;• Symfi (EFV 600 mg/ TDF/3TC)&lt;br&gt;• Symfi Lo (EFV 400 mg/ TDF/3TC)&lt;br&gt;• Triumeq (DTG/ABC/3TC)</td>
<td>Epivir:&lt;br&gt;• 3TC 300 mg once daily, or&lt;br&gt;• 3TC 150 mg twice daily&lt;br&gt;See <em>Appendix B, Tables 1 and 2</em> for dosing information for FDC tablets that contain 3TC.</td>
<td>70% of 3TC dose is excreted renally&lt;br&gt;See <em>Appendix B, Table 10</em> for dose recommendations in patients with renal insufficiency.</td>
<td>5–7 hours/18–22 hours</td>
<td>Minimal toxicity&lt;br&gt;Severe acute exacerbation of hepatitis may occur in patients with HBV/HIV coinfection who discontinue 3TC.</td>
</tr>
<tr>
<td><strong>Tenofovir Alafenamide</strong> (TAF) <em>Vemlidy</em>&lt;br&gt;Note: Vemlidy is available as a 25-mg tablet for the treatment of HBV.</td>
<td>FDC Tablets that Contain TAF:&lt;br&gt;• Descovy (TAF/FTC)&lt;br&gt;STRs that Contain TAF:&lt;br&gt;• Biktarvy (BIC/TAF/FTC)&lt;br&gt;• Genvoya (EVG/c/TAF/FTC)&lt;br&gt;• Odefsey (RPV/TAF/FTC)&lt;br&gt;• Symtuza (DRV/c/TAF/FTC)</td>
<td>See <em>Appendix B, Tables 1 and 2</em> for dosing information for FDC tablets that contain TAF.</td>
<td>Metabolized by cathepsin A. See <em>Appendix B, Table 10</em> for dosing recommendations in patients with renal insufficiency.</td>
<td>0.5 hours/150–180 hours</td>
<td>Renal insufficiency, Fanconi syndrome, and proximal renal tubulopathy are less likely to occur with TAF than with TDF. Osteomalacia and decreases in BMD are less likely to occur with TAF than with TDF. Severe acute exacerbation of hepatitis may occur in patients with HBV/HIV coinfection who discontinue TAF. Diarrhea, nausea, headache</td>
</tr>
</tbody>
</table>
### Appendix B, Table 3. Characteristics of Nucleoside Reverse Transcriptase Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 3 of 4)

<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/ Intracellular Half-Lives</th>
<th>Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tenofovir Disoproxil Fumarate (TDF)</td>
<td>Viread</td>
<td>Viread:</td>
<td>TDF 300 mg once daily, or</td>
<td>Renal excretion is the primary route of elimination. See Appendix B, Table 10 for dose recommendations in patients with renal insufficiency.</td>
<td>17 hours/&gt;60 hours</td>
<td>Renal insufficiency, Fanconi syndrome, proximal renal tubulopathy</td>
</tr>
<tr>
<td>Note: Generic product is available.</td>
<td></td>
<td>7.5 level scoops of oral powder once daily (dosing scoop dispensed with each bottle; one 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.</td>
<td></td>
<td></td>
<td></td>
<td>Osteomalacia, decrease in BMD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>See Appendix B, Tables 1 and 2 for dosing information for FDC tablets that contain TDF.</td>
<td></td>
<td></td>
<td></td>
<td>Severe acute exacerbation of hepatitis may occur in patients with HBV/HIV coinfection who discontinue TDF.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Asthenia, headache, diarrhea, nausea, vomiting, flatulence</td>
</tr>
<tr>
<td></td>
<td></td>
<td>FDC Tablets that Contain TDF:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cimduo (TDF/3TC)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Temixys (TDF/3TC)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Truvada (TDF/FTC)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zidovudine (ZDV)</td>
<td>Retrovir</td>
<td>Zidovudine (ZDV)</td>
<td>Metabolized to GAZT</td>
<td>Renal excretion of GAZT</td>
<td>1.1 hours/ 7 hours</td>
<td>Macrocytic anemia</td>
</tr>
<tr>
<td>Note: Generic products are available.</td>
<td></td>
<td></td>
<td></td>
<td>See Appendix B, Table 10 for dosing recommendations in patients with renal insufficiency.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Retrovir:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 100 mg capsule</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 10 mg/mL IV solution</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FDC Tablets that Contain ZDV:</td>
<td></td>
<td>10 mg/mL oral solution</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 300 mg tablet</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Also available as FDC with 3TC and 3TC/ABC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Combivir (ZDV/3TC)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Trizivir (ABC/ZDV/3TC)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix B, Table 3. Characteristics of Nucleoside Reverse Transcriptase Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 4 of 4)

For dose adjustments in patients with renal or hepatic insufficiency, see Appendix B, Table 10. When no food restriction is listed, the ARV drug can be taken with or without food.

Also see Table 17.

See Appendix B, Table 2 for information about these formulations.

See Appendix B, Table 1 for information about these formulations.

Key: 3TC = lamivudine; ABC = abacavir; BIC = bictegravir; BMD = bone mineral density; CrCl = creatinine clearance; d4T = stavudine; ddl = didanosine; DOR = doravirine; DRV/c = darunavir/cobicistat; DTG = dolutegravir; EC = enteric coated; EFV = efavirenz; EVG/c = elvitegravir/cobicistat; FDC = fixed-dose combination; FDA = Food and Drug Administration; FTC = emtricitabine; GAZT = azidothymidine glucuronide; HBV = hepatitis B virus; HLA = human leukocyte antigen; HSR = hypersensitivity reaction; IV = intravenous; MI = myocardial infarction; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; WHO = World Health Organization; ZDV = zidovudine
The older NNRTI DLV is no longer commonly used in clinical practice and is not listed this table. Please refer to the FDA product label for DLV for information regarding this drug.

<table>
<thead>
<tr>
<th>Generic Name (Abbreviations) Trade Name</th>
<th>Formulations</th>
<th>Dosing Recommendationsa</th>
<th>Elimination/Metabolic Pathway</th>
<th>Serum Half-Life</th>
<th>Adverse Eventsb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doravirine (DOR) Pifeltro</td>
<td>Pifeltro:</td>
<td>One tablet once daily</td>
<td>CYP3A4/5 substrate</td>
<td>15 hours</td>
<td>Nausea</td>
</tr>
<tr>
<td></td>
<td>• 100 mg tablet</td>
<td>See Appendix B, Table 1 for dosing information for Pifeltro.</td>
<td></td>
<td></td>
<td>Dizziness</td>
</tr>
<tr>
<td></td>
<td>Also available as part of the STR Delstrigo (DOR/TDF/3TC)c</td>
<td></td>
<td></td>
<td></td>
<td>Abnormal dreams</td>
</tr>
<tr>
<td>Efavirenz (EFV) Sustiva</td>
<td>Sustiva:</td>
<td>EFV 600 mg once daily, at or before bedtime</td>
<td>Metabolized by CYP2B6 (primary), 3A4, and 2A6</td>
<td>40–55 hours</td>
<td>Rashd</td>
</tr>
<tr>
<td></td>
<td>• 50 and 200 mg capsules</td>
<td>Take on an empty stomach to reduce side effects.</td>
<td>CYP3A4 mixed inducer/inhibitor (more an inducer than an inhibitor)</td>
<td></td>
<td>Neuropsychiatric symptoms#</td>
</tr>
<tr>
<td></td>
<td>• 600 mg tablet</td>
<td>See Appendix B, Table 1 for dosing information for STRs that contain EFV.</td>
<td>CYP2B6 and 2C19 inducer</td>
<td></td>
<td>Serum transaminase elevations</td>
</tr>
<tr>
<td></td>
<td>Generic:</td>
<td></td>
<td></td>
<td></td>
<td>Hyperlipidemia</td>
</tr>
<tr>
<td></td>
<td>• 600 mg tablet</td>
<td></td>
<td></td>
<td></td>
<td>Use of EFV may lead to false-positive results with some cannabinoid and benzodiazepine screening assays.</td>
</tr>
<tr>
<td></td>
<td>STRs that Contain EFV:</td>
<td></td>
<td></td>
<td></td>
<td>QT interval prolongation</td>
</tr>
<tr>
<td></td>
<td>• Atripla (EFV/TDF/FTC)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Symfi (EFV 600 mg/ TDF/3TC)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Symfi Lo (EFV 400 mg/ TDF/3TC)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Etravirine (ETR) Intelence</td>
<td>Intelence:</td>
<td>ETR 200 mg twice daily, Take following a meal.</td>
<td>CYP3A4, 2C9, and 2C19 substrate</td>
<td>41 hours</td>
<td>Rash, including Stevens-Johnson syndromee</td>
</tr>
<tr>
<td></td>
<td>• 25, 100, and 200 mg tablets</td>
<td></td>
<td>CYP3A4 inducer CYP2C9 and 2C19 inhibitor</td>
<td></td>
<td>HSRs, characterized by rash, constitutional findings, and sometimes organ dysfunction (including hepatic failure), have been reported.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Nausea</td>
</tr>
</tbody>
</table>
### Appendix B, Table 4. Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors  
**Last updated December 18, 2019; last reviewed December 18, 2019**  
(page 2 of 2)

<table>
<thead>
<tr>
<th>Generic Name (Abbreviations) 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>
</table>
| Nevirapine (NVP) Viramune or Viramune XR | **Viramune:**  
- 200 mg tablet  
- 50 mg/5 mL oral suspension  
**Viramune XR:**  
- 400 mg tablet  
**Generic:**  
- 200 mg tablet  
- 400 mg extended release tablet  
- 50 mg/5 mL oral suspension  | **Viramune:**  
- NVP 200 mg once daily for 14 days (lead-in period); thereafter, NVP 200 mg twice daily, or  
- NVP 400 mg (Viramune XR tablet) once daily  
Take without regard to meals.  
Repeat lead-in period if therapy is discontinued for >7 days.  
In patients who develop mild-to-moderate rash without constitutional symptoms, continue lead-in dose until rash resolves, but do not extend lead-in period beyond 28 days total.  
| CYP450 substrate  
CYP3A4 and 2B6 inducer  
**Contraindicated** in patients with moderate to severe hepatic impairment.  
Dose adjustment is recommended in patients on hemodialysis (see Appendix B, Table 10).  
| 25–30 hours | Rash, including Stevens-Johnson syndrome<sup>d</sup>  
**Symptomatic Hepatitis:**  
- Symptomatic hepatitis, including fatal hepatic necrosis, has been reported.  
- Rash has been reported in approximately 50% of cases.  
- Symptomatic hepatitis occurs at a significantly higher frequency in ARV-naive female patients with pre-NVP CD4 counts >250 cells/mm<sup>3</sup> and in ARV-naive male patients with pre-NVP CD4 counts >400 cells/mm<sup>3</sup>.  
- NVP should not be initiated in these patients unless the benefit clearly outweighs the risk.  |
| Rilpivirine (RPV) Edurant | **Edurant:**  
- 25 mg tablet  
**STRs that Contain RPV:**<sup>c</sup>  
- Complera (RPV/TDF/FTC)  
- Juluca (DTG/RPV)  
- Odefsey (RPV/TAF/FTC)  | **Edurant:**  
- RPV 25 mg once daily  
Take with a meal.  
See Appendix B, Table 1 for dosing information for STRs that contain RPV.  
| CYP3A4 substrate  
| 50 hours | Rash<sup>d</sup>  
Depression, insomnia, headache  
Hepatotoxicity  
QT interval prolongation  |

<sup>a</sup> For dose adjustments in patients with renal or hepatic insufficiency, see Appendix B, Table 10. When no food restriction is listed, the ARV drug can be taken with or without food.

<sup>b</sup> Also see Table 17.

<sup>c</sup> See Appendix B, Table 1 for information about these formulations.

<sup>d</sup> Rare cases of Stevens-Johnson syndrome have been reported with the use of most NNRTIs; the highest incidence of rash was seen among patients who were receiving NVP.

<sup>e</sup> Adverse events can include dizziness, somnolence, insomnia, abnormal dreams, depression, suicidality (e.g., suicide, suicide attempt or ideation), confusion, abnormal thinking, impaired concentration, amnesia, agitation, depersonalization, hallucinations, and euphoria. Approximately 50% of patients who are receiving EFV may experience any of these symptoms. Symptoms usually subside spontaneously after 2–4 weeks, but discontinuation of EFV may be necessary in a small percentage of patients. Late-onset neurotoxicities, including ataxia and encephalopathy, have been reported.

Key: 3TC = lamivudine; ARV = antiretroviral; CD4 = CD4 T lymphocyte; CYP = cytochrome P; DLV = delavirdine; DOR = doravirine; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; FDC = fixed-dose combination; FTC = emtricitabine; HSR = hypersensitivity reaction; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; XR = extended release
Appendix B, Table 5. Characteristics of Protease Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 1 of 4)

The older PIs FPV, IDV, NFV, SQV, and TPV are no longer commonly used in clinical practice and have been removed from this table. Please refer to the July 10, 2019 version of the guidelines (found in the archived guidelines section of AIDSinfo) or to the FDA product labels for information regarding these drugs.

<table>
<thead>
<tr>
<th>Generic Name (Abbreviations)</th>
<th>Formulations</th>
<th>Dosing Recommendationsa</th>
<th>Elimination/ Metabolic Pathway</th>
<th>Serum Half-Life</th>
<th>Adverse Eventsb</th>
</tr>
</thead>
</table>
| **Atazanavir** (ATV) Reyataz (ATV/c) Evotaz | **Note:** Generic products of ATV are available. Reyataz: • 150, 200, and 300 mg capsules • 50 mg oral powder/packet **Generic:** • 100, 150, 200, and 300 mg capsules **Evotaz:** • ATV 300 mg/ COBI 150 mg tablet | Reyataz
*In ARV-Naive Patients:* • (ATV 300 mg plus RTV 100 mg) once daily; or • ATV 400 mg once daily • Take with food.

*With TDF or in ARV-Experienced Patients:* • (ATV 300 mg plus RTV 100 mg) once daily • Unboosted ATV is not recommended. • Take with food.

*With EFV in ARV-Naive Patients:* • (ATV 400 mg plus RTV 100 mg) once daily • Take with food. Evotaz:
• One tablet once daily
• Take with food.

*The use of ATV/c is not recommended* for patients who are taking TDF and who have baseline CrCl <70 mL/min (see Appendix B, Table 10 for the equation for calculating CrCl).

For dosing recommendations for patients who are also receiving H2 antagonists and PPIs, refer to Table 21a. | ATV:
• CYP3A4 inhibitor and substrate
• Weak CYP2C8 inhibitor
• UGT1A1 inhibitor COBI:
• CYP3A inhibitor and substrate
• CYP2D6 inhibitor

Dose adjustment is recommended in patients with hepatic insufficiency (see Appendix B, Table 10). | 7 hours | Indirect hyperbilirubinemia
PR interval prolongation. First degree symptomatic AV block has been reported. Use with caution in patients who have underlying conduction defects or who are on concomitant medications that can cause PR prolongation.

Cholelithiasis
Nephrolithiasis
Renal insufficiency
Serum transaminase elevations
Hyperlipidemia (especially with RTV boosting)
Skin rash
Hyperglycemia
Fat maldistribution
An increase in serum creatinine may occur when ATV is administered with COBI.
### Appendix B, Table 5. Characteristics of Protease Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019)

<table>
<thead>
<tr>
<th>Generic Name (Abbreviations)</th>
<th>Trade Name</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>Adverse Events&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Darunavir (DRV)</td>
<td>Prezista</td>
<td>Prezista: • 75, 150, 600, and 800 mg tablets • 100 mg/mL oral suspension Prezcobix: • DRV 800 mg/COBI 150 mg tablet Also available as part of the STR Symtuza (DRV/c/TAF/FTC)</td>
<td>Prezista In ARV-Naive Patients or ARV-Experienced Patients with No DRV Mutations: • (DRV 800 mg plus RTV 100 mg) once daily • Take with food. In ARV-Experienced Patients with One or More DRV Resistance Mutations: • (DRV 600 mg plus RTV 100 mg) twice daily • Take with food. Unboosted DRV is not recommended. Prezcobix: • One tablet once daily • Take with food. <strong>Not recommended</strong> for patients with one or more DRV resistance-associated mutations. • Coadministering Prezcobix and TDF is not recommended for patients with baseline CrCl &lt;70 mL/min (see Appendix B, Table 10 for the equation for calculating CrCl). See Appendix B, Table 1 for dosing information for Symtuza.</td>
<td>DRV: • CYP3A4 inhibitor and substrate • CYP2C9 inducer COBI: • CYP3A inhibitor and substrate • CYP2D6 inhibitor</td>
<td>15 hours when combined with RTV 7 hours when combined with COBI</td>
<td>Skin Rash: DRV has a sulfonamide moiety, however incidence and severity of rash are similar in those with or without a sulfonamide allergy; 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 An increase in serum creatinine may occur when DRV is administered with COBI.</td>
</tr>
</tbody>
</table>
### Appendix B, Table 5. Characteristics of Protease Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 3 of 4)

<table>
<thead>
<tr>
<th>Generic Name (Abbreviations)</th>
<th>Formulations</th>
<th>Dosing Recommendations&lt;br&gt;Note: LPV is only available as a component of an FDC tablet that also contains RTV.</th>
<th>Elimination/ Metabolic Pathway</th>
<th>Serum Half-Life</th>
<th>Adverse Events&lt;br&gt;Note: LPV is only available as a component of an FDC tablet that also contains RTV.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lopinavir/ Ritonavir (LPV/r)</td>
<td>Kaletra:</td>
<td>• LPV/r 200 mg/50 mg tablets&lt;br&gt;• LPV/r 100 mg/25 mg tablets&lt;br&gt;• LPV/r 400 mg/100 mg per 5 mL of oral solution. Oral solution contains 42% alcohol.</td>
<td>CYP3A4 inhibitor and substrate</td>
<td>5–6 hours</td>
<td>GI intolerance, nausea, vomiting, diarrhea&lt;br&gt;Pancreatitis&lt;br&gt;Hyperlipidemia (especially hypertriglyceridemia)&lt;br&gt;Serum transaminase elevation&lt;br&gt;Hyperglycemia&lt;br&gt;Insulin resistance/diabetes mellitus&lt;br&gt;Fat maldistribution&lt;br&gt;Possible increase in the frequency of bleeding episodes in patients with hemophilia&lt;br&gt;PR interval prolongation&lt;br&gt;QT interval prolongation and Torsades de Pointes have been reported; however, causality could not be established.</td>
</tr>
<tr>
<td>Note: Kaletra is only available as a component of a FDC tablet that also contains RTV.</td>
<td>Kaletra:</td>
<td>• LPV/r 400 mg/100 mg twice daily, or&lt;br&gt;• LPV/r 800 mg/200 mg once daily. However, once-daily dosing is not recommended for patients with three or more LPV-associated mutations, pregnant women, or patients receiving EFV, NVP, carbamazepine, phenytoin, or phenobarbital.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Kaletra:</td>
<td>• LPV/r 533 mg/133 mg oral solution twice daily</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Kaletra:</td>
<td><strong>Food Restrictions</strong>&lt;br&gt;<strong>Tablet:</strong>&lt;br&gt;• Take without regard to meals.&lt;br&gt;<strong>Oral Solution:</strong>&lt;br&gt;• Take with food.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Kaletra:</td>
<td><strong>With EFV or NVP in PI-Naive or PI Experienced Patients:</strong>&lt;br&gt;• LPV/r 500 mg/125 mg tablets twice daily (use a combination of two LPV/r 200 mg/50 mg tablets plus one LPV/r 100 mg/25 mg tablet to make a total dose of LPV/r 500 mg/125 mg), or&lt;br&gt;• LPV/r 533 mg/133 mg oral solution twice daily</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ritonavir (RTV)</td>
<td>Norvir</td>
<td>• 100 mg tablet&lt;br&gt;• 100 mg soft gel capsule&lt;br&gt;• 80 mg/mL oral solution. Oral solution contains 43% alcohol.&lt;br&gt;• 100 mg single packet oral powder&lt;br&gt;Also available as part of the FDC tablet Kaletra (LPV/r)</td>
<td>CYP3A4 &gt; 2D6 substrate&lt;br&gt;Potent CYP3A4 and 2D6 inhibitor&lt;br&gt;Inducer of UGT1A1 and CYPs 1A2, 2C8, 2C9, and 2C19</td>
<td>3–5 hours</td>
<td>GI intolerance, nausea, vomiting, diarrhea&lt;br&gt;Paresthesia (circumoral and extremities)&lt;br&gt;Hyperlipidemia (especially hypertriglyceridemia)&lt;br&gt;Hepatitis&lt;br&gt;Asthenia&lt;br&gt;Taste perversion&lt;br&gt;Hyperglycemia&lt;br&gt;Fat maldistribution&lt;br&gt;Possible increase in the frequency of bleeding episodes in patients with hemophilia</td>
</tr>
<tr>
<td>Note: Norvir is available. Although RTV was initially developed as a PI for HIV treatment, RTV is currently used at a lower dose of 100 mg to 200 mg once or twice daily as a PK enhancer to increase the concentrations of other PIs.</td>
<td>Norvir</td>
<td>• 100 mg tablet&lt;br&gt;• 100 mg soft gel capsule&lt;br&gt;• 80 mg/mL oral solution. Oral solution contains 43% alcohol.&lt;br&gt;• 100 mg single packet oral powder&lt;br&gt;Also available as part of the FDC tablet Kaletra (LPV/r)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Norvir</td>
<td><strong>As a PK Booster (or Enhancer) for Other PIs:</strong>&lt;br&gt;• RTV 100–400 mg per day in one or two divided doses (refer to other PIs for specific dosing recommendations).</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Norvir</td>
<td><strong>Food Restrictions</strong>&lt;br&gt;<strong>Tablet:</strong>&lt;br&gt;• Take with food.&lt;br&gt;<strong>Capsule and Oral Solution:</strong>&lt;br&gt;• To improve tolerability, take with food if possible.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix B, Table 5. Characteristics of Protease Inhibitors *(Last updated December 18, 2019; last reviewed December 18, 2019)* (page 4 of 4)

a For dose adjustments in patients with hepatic insufficiency, see Appendix B, Table 10.

b Also see Table 17.

**Key:**
- ARV = antiretroviral
- ATV = atazanavir
- ATV/c = atazanavir/cobicistat
- AV = atrioventricular
- COBI = cobicistat
- CrCl = creatinine clearance
- CYP = cytochrome P
- DRV = darunavir
- DRV/c = darunavir/cobicistat
- EFV = efavirenz
- FDA = Food and Drug Administration
- FDC = fixed-dose combination
- FPV = fosamprenavir
- FTC = emtricitabine
- GI = gastrointestinal
- IDV = indinavir
- LPV = lopinavir
- LPV/r = lopinavir/ritonavir
- msec = millisecond
- NFV = nelfinavir
- NVP = nevirapine
- PI = protease inhibitor
- PK = pharmacokinetic
- PPI = proton pump inhibitor
- RTV = ritonavir
- SQV = saquinavir
- STR = single-tablet regimen
- TAF = tenofovir alafenamide
- TDF = tenofovir disoproxil fumarate
- TPV = tipranavir
- UGT = uridine diphosphate glucuronyl transferase

---

Downloaded from https://aidsinfo.nih.gov/guidelines on 7/3/2020
Appendix B, Table 6. Characteristics of Integrase Strand Transfer Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019)  
(page 1 of 2)

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation)</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><strong>Bictegravir</strong> (BIC)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>BIC is only available as a component of the STR Biktarvy (BIC/TAF/FTC).</td>
<td>Biktarvy: One tablet PO once daily</td>
<td>CYP3A4 substrate UGT1A1-mediated glucuronidation</td>
<td>~17 hours</td>
<td>Diarrhea, Nausea, Headache, Weight gain</td>
</tr>
<tr>
<td><strong>Dolutegravir</strong> (DTG) <strong>Tivicay</strong></td>
<td>Tivicay: 50 mg tablet</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>STRs that Contain DTG:c</td>
<td>STRs that Contain DTG:c</td>
<td>In ARV-Naive or ARV-Experienced, INSTI-Naive Patients: DTG 50 mg PO once daily</td>
<td>UGT1A1-mediated glucuronidation Minor substrate of CYP3A4</td>
<td>~14 hours</td>
<td>Insomnia, Headache, Depression and suicidal ideation (rare; usually occurs in patients with pre-existing psychiatric conditions), Weight gain, Hepatotoxicity. There is a potential increased risk of NTDs in infants born to individuals who received DTG around the time of conception (see Table 6b for more information). HSRs, including rash, constitutional symptoms, and organ dysfunction (including liver injury), have been reported.</td>
</tr>
<tr>
<td>Elvitegravir (EVG)</td>
<td>EVG is only available as a component of an STR tablet that also contains COBI, FTC, and either TDF or TAF. STRs that Contain EVG:c</td>
<td>Genvoya: One tablet PO once daily with food See Appendix B, Table 10 for recommendations on dosing in persons with renal insufficiency.</td>
<td>CYP3A and UGT1A1/3 substrate COBI: CYP3A inhibitor and substrate CYP2D6 inhibitor</td>
<td>EVG/c: ~13 hours</td>
<td>Nausea, Diarrhea, Depression and suicidal ideation (rare; usually occurs in patients with pre-existing psychiatric conditions)</td>
</tr>
</tbody>
</table>
### Appendix B, Table 6. Characteristics of Integrase Strand Transfer Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019)

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation) Trade Name</th>
<th>Formulations</th>
<th>Dosing Recommendations&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Elimination/ Metabolic Pathways</th>
<th>Serum Half-Life</th>
<th>Adverse Events&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Raltegravir (RAL)</strong> Isentress Isentress HD</td>
<td><strong>Isentress:</strong></td>
<td>400 mg tablet • 25 and 100 mg chewable tablets • 100 mg single-use packet for oral suspension</td>
<td><strong>Isentress</strong> In ARV-Naive Patients or ARV-Experienced Patients: • 400 mg PO twice daily With Rifampin: • 800 mg twice daily</td>
<td>UGT1A1-mediated glucuronidation</td>
<td>~9 hours</td>
</tr>
<tr>
<td></td>
<td><strong>Isentress HD:</strong></td>
<td>600 mg tablet</td>
<td><strong>Isentress HD</strong> In ARV-Naive or ARV-Experienced Patients with Virologic Suppression on a Regimen containing RAL 400 mg Twice Daily: • 1,200 mg (two 600-mg tablets) PO once daily With Rifampin: • Not recommended</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> For dose adjustments in patients with hepatic insufficiency, see Appendix B, Table 10. When no food restriction is listed, the ARV drug can be taken with or without food.

<sup>b</sup> Also see Table 17.

Key: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; BIC = bictegravir; COBI = cobicistat; CPK = creatine phosphokinase; CYP = cytochrome P; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FDC = fixed-dose combination; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; HSR = hypersensitivity reaction; INSTI = integrase strand transfer inhibitor; NTD = neural tube defect; PO = orally; RAL = raltegravir; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV/r = tipranavir/ritonavir; UGT = uridine diphosphate glucuronyl transferase

### Appendix B, Table 7. Characteristics of the Fusion Inhibitor (Last updated December 18, 2019; last reviewed December 18, 2019)

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation) Trade Name</th>
<th>Formulation</th>
<th>Dosing Recommendation</th>
<th>Serum Half-Life</th>
<th>Elimination</th>
<th>Adverse Events&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Enfuvirtide (T-20)</strong> Fuzeon</td>
<td>Fuzeon: • Injectable; supplied as lyophilized powder. • Each vial contains 108 mg of T-20; reconstitute with 1.1 mL of sterile water for injection for delivery of approximately 90 mg/1 mL. • Refer to prescribing information for storage instruction.</td>
<td>T-20 90 mg/1 mL SQ twice daily</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>Local injection site reactions (e.g., pain, erythema, induration, nodules and cysts, pruritus, ecchymosis) in almost 100% of patients Increased incidence of bacterial pneumonia HSR occurs in &lt;1% of patients. Symptoms may include rash, fever, nausea, vomiting, chills, rigors, hypotension, or elevated serum transaminases. Re-challenge is not recommended.</td>
</tr>
</tbody>
</table>

<sup>a</sup> Also see Table 17.

Key: HSR = hypersensitivity reaction; SQ = subcutaneous; T-20 = enfuvirtide

*Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV*
Appendix B, Table 8. Characteristics of the CCR5 Antagonist  (Last updated December 18, 2019; last reviewed December 18, 2019)

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation) Trade Name</th>
<th>Formulation</th>
<th>Dosing Recommendationsa</th>
<th>Serum Half-Life</th>
<th>Elimination/Metabolic Pathway</th>
<th>Adverse Eventsb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maraviroc (MVC) Selzentry</td>
<td>Selzentry:  • 150 and 300 mg tablets</td>
<td>Selzentry:  • MVC 150 mg PO twice daily when given with drugs that are strong CYP3A inhibitors (with or without CYP3A inducers), including PIs (except TPV/r)  • MVC 300 mg PO twice daily when given with NRTIs, T-20, TPV/r, NVP, RAL, and other drugs that are not strong CYP3A inhibitors or inducers  • MVC 600 mg PO twice daily when given with drugs that are CYP3A inducers, including EFV, ETR, etc. (without a CYP3A inhibitor) Take MVC without regard to meals.</td>
<td>14–18 hours</td>
<td>CYP3A4 substrate</td>
<td>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</td>
</tr>
</tbody>
</table>

a For dose adjustments in patients with hepatic insufficiency, see Appendix B, Table 10.
b Also see Table 17.

Key: CYP = cytochrome P; EFV = efavirenz; ETR = etravirine; MVC = maraviroc; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PO = orally; RAL = raltegravir; T-20 = enfuvirtide; TPV/r = tipranavir/ritonavir

Appendix B, Table 9. Characteristics of the CD4 Post-Attachment Inhibitor  (Last updated December 18, 2019; last reviewed December 18, 2019)

<table>
<thead>
<tr>
<th>Generic Name (Abbreviation) Trade Name</th>
<th>Formulation</th>
<th>Dosing Recommendations</th>
<th>Serum Half-Life</th>
<th>Elimination/ Metabolic Pathway</th>
<th>Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibalizumab (IBA) Trogarzo</td>
<td>Trogarzo: • Single-dose 2 mL vial containing 200 mg/1.33 mL (150 mg/mL) of ibalizumab</td>
<td>Trogarzo: • Administer a single loading dose of IBA 2,000 mg IV infusion over 30 minutes, followed by a maintenance dose of IBA 800 mg IV infusion over 15 minutes every 2 weeks.  • See prescribing information for additional instructions for preparing, storing, and administering IBA, and for monitoring patients who are receiving IBA.</td>
<td>~64 hours</td>
<td>Not well defined</td>
<td>Diarrhea  Dizziness  Nausea  Rash</td>
</tr>
</tbody>
</table>

Key: IBA = ibalizumab; IV = intravenous
The older ARV drugs ddI, d4T, FPV, IDV, NFV, SQV, and TPV are no longer commonly used in clinical practice and have been removed from this table. Please refer to the July 10, 2019, guidelines in the Guidelines Archive section of AIDSinfo or to the FDA product labels for these drugs for recommendations on dosing in persons with renal or hepatic insufficiency.

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 (Abbreviations)</th>
<th>Usual Daily Dosea</th>
<th>Dosing in Persons with Renal Insufficiency</th>
<th>Dosing in Persons with Hepatic Impairment</th>
</tr>
</thead>
</table>
| **Abacavir (ABC) Ziagen**    | ABC 300 mg PO twice daily or ABC 600 mg PO once daily | No dose adjustment necessary. | Brain-Pugh Class A: ABC 200 mg PO twice daily (use oral solution)  
Child-Pugh Class B or C: Contraindicated |
| **Emtricitabine (FTC) Emtriva** | FTC 200 mg oral capsule once daily or FTC 240 mg (24 mL) oral solution once daily | Dose by Formulation | No dose recommendation. |
|                              |                  | CrCl (mL/min) | Capsule | Solution |
|                              |                  | 30–49 | 200 mg every 48 hours | 120 mg every 24 hours |
|                              |                  | 15–29 | 200 mg every 72 hours | 80 mg every 24 hours |
|                              |                  | <15   | 200 mg every 96 hours | 60 mg every 24 hours |
|                              |                  | On HDa | 200 mg every 24 hours | 240 mg every 24 hours |
| **Lamivudine (3TC) Epivir**  | 3TC 300 mg PO once daily or 3TC 150 mg PO twice daily | CrCl (mL/min) | Dose |
|                              |                  | 30–49 | 150 mg every 24 hours |
|                              |                  | 15–29 | 1 x 150 mg, then 100 mg every 24 hours |
|                              |                  | 5–14  | 1 x 150 mg, then 50 mg every 24 hours |
|                              |                  | <5 or on HDa | 1 x 50 mg, then 25 mg every 24 hours |
| **Tenofovir Alafenamide (TAF) Vemlidy** | Vemlidy is available as a 25-mg tablet for the treatment of HBV. | CrCl (mL/min) | Dose |
|                              |                  | <15 and not on HD | Not recommended |
|                              |                  | On HDa | One tablet once daily |

Some FDC products are not recommended in persons with different degrees of renal insufficiency. The recommendations for individual FDCs based on CrCl level are outlined below.

- **CrCl <70 mL/min:** Initiation of Striibild is not recommended.
- **CrCl <50 mL/min:** FDCs not recommended: Atripla, Combivir, Complera, Delstrigo, Dovato, Epzicom, Triumeq, or Trizivir.
- **CrCl <30 mL/min:** FDCs not recommended: Biktavy and Truvada.
- **CrCl <30 mL/min and not on HD:** FDCs not recommended: Descovy, Genvoya, Odefsey, and Symtuza.

The component drugs in some of the FDC products listed above may be prescribed as individual formulations with dose adjustment based on CrCl level as indicated below in this table.

---

Appendix B, Table 10. Antiretroviral Dosing Recommendations in Persons with Renal or Hepatic Insufficiency (Last updated December 18, 2019; last reviewed December 18, 2019) (page 1 of 6)
### Appendix B, Table 10. Antiretroviral Dosing Recommendations in Persons with Renal or Hepatic Insufficiency (Last updated December 18, 2019; last reviewed December 18, 2019)

#### NRTIs, continued

<table>
<thead>
<tr>
<th>Generic Name (Abbreviations) Trade Name</th>
<th>Usual Daily Dosea</th>
<th>Dosing in Persons with Renal Insufficiency</th>
<th>Dosing in Persons with Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tenofovir Alafenamide/Emtricitabine (TAF/FTC) Descovy</strong></td>
<td>TAF for HIV treatment is only available as a component of FDC tablets (i.e., in Descovy, Genvoya, Odefsey, Biktarvy, and Symtuza). TAF 10 mg PO daily with EVG/c (Genvoya) or DRV/c (Symtuza) TAF 25 mg PO daily in other FDC tablets</td>
<td><strong>CrCl (mL/min)</strong></td>
<td><strong>Dose</strong></td>
</tr>
<tr>
<td><strong>NRTIs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Tenofovir Disoproxil Fumarate (TDF) Viread</strong></td>
<td>TDF 300 mg PO once daily</td>
<td><strong>CrCl (mL/min)</strong></td>
<td><strong>Dose</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>30–49</td>
<td>300 mg every 48 hours</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10–29</td>
<td>300 mg twice weekly (every 72–96 hours)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;10 and not on HD</td>
<td>No recommendation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>On HD</td>
<td>300 mg every 7 days</td>
</tr>
<tr>
<td><strong>Tenofovir Disoproxil Fumarate/Emtricitabine (TDF/FTC) Truvada</strong></td>
<td>One tablet PO once daily</td>
<td><strong>CrCl (mL/min)</strong></td>
<td><strong>Dose</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>30–49</td>
<td>One tablet every 48 hours</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;30 or on HD</td>
<td>Not recommended</td>
</tr>
<tr>
<td><strong>Zidovudine (ZDV) Retrovir</strong></td>
<td>ZDV 300 mg PO twice daily</td>
<td><strong>CrCl (mL/min)</strong></td>
<td><strong>Dose</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;15 or on HD</td>
<td>100 mg three times a day or 300 mg once daily</td>
</tr>
</tbody>
</table>

#### NNRTIs

<table>
<thead>
<tr>
<th>Generic Name (Abbreviations) Trade Name</th>
<th>Usual Daily Dosea</th>
<th>Dosing in Persons with Renal Insufficiency</th>
<th>Dosing in Persons with Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Doravirine (DOR) Pifeltro</strong></td>
<td>One tablet PO once daily</td>
<td>No dose adjustment required in mild, moderate, or severe renal impairment. Has not been studied in individuals with ESRD or on HD.</td>
<td><strong>Child-Pugh Class A or B:</strong> No dose adjustment  <strong>Child-Pugh Class C:</strong> Not studied</td>
</tr>
<tr>
<td><strong>Doravirine/Tenofovir Disoproxil Fumarate/Lamivudine (DOR/TDF/3TC) Delstrigo</strong></td>
<td>One tablet PO once daily</td>
<td><strong>Not recommended</strong> if CrCl &lt;50 mL/min.</td>
<td><strong>Child-Pugh Class A or B:</strong> No dose adjustment  <strong>Child-Pugh Class C:</strong> Not studied</td>
</tr>
</tbody>
</table>
### Appendix B, Table 10. Antiretroviral Dosing Recommendations in Persons with Renal or Hepatic Insufficiency
(Last updated December 18, 2019; last reviewed December 18, 2019)

<table>
<thead>
<tr>
<th>Generic Name (Abbreviations)</th>
<th>Usual Daily Dose</th>
<th>Dosing in Persons with Renal Insufficiency</th>
<th>Dosing in Persons with Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NNRTIs, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Efavirenz (EFV)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sustiva</strong></td>
<td>EFV 600 mg PO once daily on an empty stomach, preferably at bedtime</td>
<td>No dose adjustment necessary.</td>
<td>No dose recommendation; use with caution in patients with hepatic impairment.</td>
</tr>
<tr>
<td><strong>Efavirenz/Tenofovir Disoproxil Fumarate/Emtricitabine (EFV/TDF/FTC)</strong></td>
<td>One tablet PO once daily on an empty stomach, preferably at bedtime</td>
<td><strong>Not recommended</strong> if CrCl &lt;50 mL/min. Instead, use the individual component ARVs and adjust TDF and FTC doses according to CrCl level.</td>
<td>No dose recommendation; use with caution in patients with hepatic impairment.</td>
</tr>
<tr>
<td><strong>Atripla</strong></td>
<td>One tablet PO once daily on an empty stomach, preferably at bedtime</td>
<td><strong>Not recommended</strong> if CrCl &lt;50 mL/min or if patient is on HD. Instead, use the individual component ARVs and adjust TDF and 3TC doses according to CrCl level.</td>
<td><strong>Not recommended</strong> for patients with moderate or severe hepatic impairment. Use with caution in patients with mild hepatic impairment.</td>
</tr>
<tr>
<td><strong>Efavirenz 400 mg/ Tenofovir Disoproxil Fumarate/Lamivudine (EFV/TDF/3TC)</strong></td>
<td>One tablet once daily on an empty stomach, preferably at bedtime</td>
<td><strong>Not recommended</strong> if CrCl &lt;50 mL/min or if patient is on HD. Instead, use the individual component ARVs and adjust TDF and 3TC doses according to CrCl level.</td>
<td><strong>Not recommended</strong> for patients with moderate or severe hepatic impairment. Use with caution in patients with mild hepatic impairment.</td>
</tr>
</tbody>
</table>
| **Symfi**                    | One tablet once daily on an empty stomach, preferably at bedtime | No dose adjustment necessary. | Child-Pugh Class A or B: No dose adjustment  
Child-Pugh Class C: No dose recommendation |
| **Efavirenz 600 mg/ Tenofovir Disoproxil Fumarate/Lamivudine (EFV/TDF/3TC)** | One tablet PO twice daily \( \text{or} \) NVP 400 mg PO once daily (using Viramune XR formulation) | No dose adjustment for patients with renal impairment.  
Patients on HD should receive an additional dose of NVP 200 mg following each dialysis treatment. | Child-Pugh Class A: No dose adjustment  
Child-Pugh Class B or C: Contraindicated |
| **Nevirapine (NVP)**         |                  |                                          |                                          |
| **Viramune** or **Viramune XR** | NVP 200 mg PO twice daily \( \text{or} \) NVP 400 mg PO once daily (using Viramune XR formulation) | No dose adjustment for patients with renal impairment.  
Patients on HD should receive an additional dose of NVP 200 mg following each dialysis treatment. | Child-Pugh Class A or B: No dose adjustment  
Child-Pugh Class C: No dose recommendation |
| **Rilpivirine (RPV)**        |                  |                                          |                                          |
| **Edurant**                  | RPV 25 mg PO once daily | No dose adjustment necessary. | Child-Pugh Class A or B: No dose adjustment  
Child-Pugh Class C: No dose recommendation |
| **Rilpivirine/Tenofovir Alafenamide/Emtricitabine (RPV/TAF/FTC)** | One tablet PO once daily | **In Patients on Chronic HD:**  
\( \text{• One tablet once daily. On HD days, administer after dialysis.} \)  
**Not recommended** in patients with CrCl <30 mL/min who are not receiving chronic HD. | Child-Pugh Class A or B: No dose adjustment  
Child-Pugh Class C: No dose recommendation |
| **Odefsey**                  | One tablet PO once daily | No dose adjustment if CrCl <50 mL/min. Instead, use the individual component ARVs and adjust TDF and FTC doses according to CrCl level. | Child-Pugh Class A or B: No dose adjustment  
Child-Pugh Class C: No dose recommendation |
| **Rilpivirine/Tenofovir Disoproxil Fumarate/Emtricitabine (RPV/TDF/FTC)** | One tablet PO once daily | **Not recommended** if CrCl <50 mL/min. Instead, use the individual component ARVs and adjust TDF and FTC doses according to CrCl level. | Child-Pugh Class A or B: No dose adjustment  
Child-Pugh Class C: No dose recommendation |
### Appendix B, Table 10. Antiretroviral Dosing Recommendations in Persons with Renal or Hepatic Insufficiency

(last updated December 18, 2019; last reviewed December 18, 2019)

<table>
<thead>
<tr>
<th>Generic Name (Abbreviations) Trade Name</th>
<th>Usual Daily Doseα</th>
<th>Dosing in Persons with Renal Insufficiency</th>
<th>Dosing in Persons with Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NNRTIs, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Rilpivirine/ Dolutegravir (RPV/DTG)    | One tablet PO once daily with food | No dose adjustment necessary. In patients with CrCl <30 mL/min, monitor closely for adverse effects. | **Child-Pugh Class A or B**: No dose adjustment  
**Child-Pugh Class C**: No dose recommendation |
| Juluca                                 |                   |                                          |                                          |
| **PIs**                                |                   |                                          |                                          |
| Atazanavir (ATV) Reyataz               | One tablet PO once daily  
or (ATV 300 mg plus RTV 100 mg) PO once daily | No dose adjustment for patients with renal dysfunction who do not require HD.  
In ARV-Naive Patients on HD:  
• (ATV 300 mg plus RTV 100 mg) once daily  
In ARV-Experienced Patients on HD:  
• ATV and ATV/r are not recommended | **Child-Pugh Class A**: No dose adjustment  
**Child-Pugh Class B**: ATV 300 mg once daily (unboosted) for ARV-naive patients only  
**Child-Pugh Class C**: Not recommended  
RTV boosting is not recommended in patients with hepatic impairment. |
| Atazanavir/Cobicistat (ATV/c) Evotaz   | One tablet PO once daily | If Used with TDF:  
• Not recommended if CrCl <70 mL/min | Not recommended in patients with hepatic impairment. |
| Darunavir (DRV) Prezista               | If In ARV-Naive Patients and ARV-Experienced Patients with No DRV Resistance Mutations:  
• (DRV 800 mg plus RTV 100 mg) PO once daily with food  
In ARV-Experienced Patients with at Least One DRV Resistance Mutation:  
• (DRV 600 mg plus RTV 100 mg) PO twice daily | No dose adjustment necessary. | **In Patients with Mild-to-Moderate Hepatic Impairment**: No dose adjustment  
**In Patients with Severe Hepatic Impairment**: Not recommended |
| Darunavir/Cobicistat (DRV/c) Prezobix  | One tablet PO once daily | If Used with TDF:  
• Not recommended if CrCl <70 mL/min | **Child-Pugh Class A or B**: No dose adjustment  
**Child-Pugh Class C**: Not recommended |
| Darunavir/ Cobicistat/Tenofovir Alafenamide/ Emtricitabine (DRV/c/TAF/FTC) Symtuza | One tablet PO once daily | **In Patients on Chronic HD**:  
• One tablet once daily. On HD days, administer after dialysis.  
**Not recommended in patients with CrCl <30 mL/min who are not receiving chronic HD**: | Not recommended for patients with severe hepatic impairment. |

---

*α Usual daily dose for adults and adolescents with normal renal and hepatic function.*
### Appendix B, Table 10. Antiretroviral Dosing Recommendations in Persons with Renal or Hepatic Insufficiency (Last updated December 18, 2019; last reviewed December 18, 2019)

<table>
<thead>
<tr>
<th>Generic Name (Abbreviations)</th>
<th>Trade Name</th>
<th>Usual Daily Dosea</th>
<th>Dosing in Persons with Renal Insufficiency</th>
<th>Dosing in Persons with Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PIs, continued</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lopinavir/Ritonavir (LPV/r)</td>
<td>Kaletra</td>
<td>(LPV/r 400 mg/100 mg) PO twice daily or (LPV/r 800 mg/200 mg) PO once daily</td>
<td>Avoid once-daily dosing in patients on HD.</td>
<td></td>
</tr>
<tr>
<td>Ritonavir (RTV)</td>
<td>Norvir</td>
<td>As a PI-Boosting Agent: • RTV 100–400 mg per day</td>
<td>No dose adjustment necessary.</td>
<td>Refer to recommendations for the primary (i.e., boosted) PI.</td>
</tr>
<tr>
<td><strong>INSTIs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bictegravir/Tenofovir</td>
<td>Biktarvy</td>
<td>One tablet once daily</td>
<td><strong>Not recommended</strong> for use in patients with CrCl &lt;30 mL/min.</td>
<td></td>
</tr>
<tr>
<td>Alafenamide/Emtricitabine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(BIC/TAF/FTC)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dolutegravir (DTG)</td>
<td>Tivicay</td>
<td>DTG 50 mg once daily or DTG 50 mg twice daily</td>
<td>No dose adjustment necessary.</td>
<td></td>
</tr>
<tr>
<td>Dolutegravir/Abacavir/Lamivudine</td>
<td>Triumeq</td>
<td>One tablet once daily</td>
<td><strong>Not recommended</strong> if CrCI &lt;50 mL/min. Instead, use the individual component drugs and adjust 3TC dose according to CrCl.</td>
<td></td>
</tr>
<tr>
<td>(DTG/ABC/3TC)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dolutegravir/Rilpivirine (DTG/RPV)</td>
<td>Juluca</td>
<td>One tablet PO once daily with food</td>
<td>No dose adjustment necessary. In patients with CrCl &lt;30 mL/min, monitor closely for adverse effects.</td>
<td></td>
</tr>
<tr>
<td>Elvitegravir/Cobicistat/Tenofovir</td>
<td>Genvoya</td>
<td>One tablet once daily</td>
<td><strong>In Patients on Chronic HD:</strong> • One tablet once daily. On HD days, administer after dialysis. <strong>Not recommended</strong> in patients with CrCl &lt;30 mL/min who are not receiving chronic HD.</td>
<td>In Patients with Mild-to-Moderate Hepatic Insufficiency: No dose adjustment necessary</td>
</tr>
<tr>
<td>Alafanamide/Emtricitabine</td>
<td></td>
<td></td>
<td></td>
<td>In Patients with Severe Hepatic Insufficiency: <strong>Not recommended</strong></td>
</tr>
<tr>
<td>(EVG/c/TAF/FTC)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elvitegravir/Cobicistat/Tenofovir</td>
<td>Stribild</td>
<td>One tablet once daily</td>
<td>EGV/c/TDF/FTC should not be initiated in patients with CrCl &lt;70 mL/min. Discontinue EGV/c/TDF/FTC if CrCl declines to &lt;50 mL/min while patient is on therapy.</td>
<td>In Patients with Mild-to-Moderate Hepatic Insufficiency: No dose adjustment necessary</td>
</tr>
<tr>
<td>Disoproxil Fumarate/Emtricitabine</td>
<td></td>
<td></td>
<td></td>
<td>In Patients with Severe Hepatic Insufficiency: <strong>Not recommended</strong></td>
</tr>
</tbody>
</table>
### Appendix B, Table 10. Antiretroviral Dosing Recommendations in Persons with Renal or Hepatic Insufficiency  
_Last updated December 18, 2019; last reviewed December 18, 2019_ (page 6 of 6)

<table>
<thead>
<tr>
<th>Generic Name (Abbreviations)</th>
<th>Usual Daily Dosea</th>
<th>Dosing in Persons with Renal Insufficiency</th>
<th>Dosing in Persons with Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>INSTIs, continued</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raltegravir (RAL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Isentress</em></td>
<td>RAL 400 mg twice daily (using Isentress formulation) or RAL 1,200 mg once daily (using Isentress HD formulation only)</td>
<td>No dose adjustment necessary.</td>
<td>In Patients with Mild-to-Moderate Hepatic Insufficiency: No dose adjustment necessary</td>
</tr>
<tr>
<td><em>Isentress HD</em></td>
<td></td>
<td></td>
<td>In Patients with Severe Hepatic Insufficiency: No recommendation</td>
</tr>
</tbody>
</table>

| **Fusion Inhibitor**         |                   |                                           |                                          |
| Enfuvirtide (T-20)           | T-20 90 mg SQ twice daily | No dose adjustment necessary. | No dose adjustment necessary. |
| *Fuzeon*                     |                   |                                           |                                          |

| **CCR5 Antagonist**          |                   |                                           |                                          |
| Maraviroc (MVC)              |                   |                                           |                                          |
| _Selzentry_                  | The recommended dose differs based on concomitant medications and potential for drug-drug interactions. See Appendix B, Table 8 for detailed dosing information. | In Patients with CrCl <30 mL/min or Patients Who Are on HD  |
|                              |                   | **Without Potent CYP3A Inhibitors or Inducers:** |
|                              |                   | • MVC 300 mg twice daily; if postural hypotension occurs, reduce to MVC 150 mg twice daily |
|                              |                   | **With Potent CYP3A Inducers or Inhibitors:** |
|                              |                   | • Not recommended |
| Maraviroc (MVC)              |                   |                                           | No dose recommendations. MVC concentrations will likely be increased in patients with hepatic impairment. |
| _Selzentry_                  |                   |                                           |                                          |
|                              |                   |                                           |                                          |

| **CD4 Post-Attachment Inhibitor** |                   |                                           |                                          |
| Ibalizumab (IBA)                |                   |                                           |                                          |
| _Trogarzo_                      | Loading dose: IBA 2,000 mg IV Maintenance dose: IBA 800 mg IV every 2 weeks | No dose adjustment recommended. | No recommendation. |
|                              |                   |                                           |                                          |

---

*a Refer to Appendix B, Tables 1–9 for additional dosing information.  
b On dialysis days, the patient should take the dose after the HD session.

**Key:** 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; ATV = atazanavir; ATP/c = atazanavir/cobicistat; ATP/r = atazanavir/ritonavir; BIC = bictegravir; CAPD = chronic ambulatory peritoneal dialysis; COBI = cobicistat; CrCl = creatinine clearance; CYP = cytochrome P; d4T = stavudine; ddl = didanosine; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DTG = dolutegravir; EC = enteric coated; EFV = efavirenz; ESRD = end stage renal disease; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FDA = Food and Drug Administration; FDC = fixed-dose combination; FPV = fosamprenavir; FTC = emtricitabine; HBV = hepatitis B virus; HD = hemodialysis; IBA = ibalizumab; IDV = indinavir; INSTI = integrase strand transfer inhibitor; IV = intravenous; LPV = lopinavir; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PO = orally; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQ = subcutaneous; SQV = saquinavir; T-20 = enfuvirtide; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV = tipranavir; XR = extended release; ZDV = zidovudine
### Child-Pugh Score

<table>
<thead>
<tr>
<th>Component</th>
<th>Points Scored</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encephalopathy&lt;sup&gt;a&lt;/sup&gt;</td>
<td>None</td>
<td>Grade 1–2</td>
<td></td>
<td>Grade 3–4</td>
</tr>
<tr>
<td>Ascites</td>
<td>None</td>
<td>Mild or controlled by diuretics</td>
<td></td>
<td>Moderate or refractory despite diuretics</td>
</tr>
<tr>
<td>Albumin</td>
<td>&gt;3.5 g/dL</td>
<td>2.8–3.5 g/dL</td>
<td></td>
<td>&lt;2.8 g/dL</td>
</tr>
<tr>
<td>Total Bilirubin, or Modified Total Bilirubin&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;2 mg/dL (&lt;34 μmol/L)</td>
<td>2–3 mg/dL (34–50 μmol/L)</td>
<td></td>
<td>&gt;3 mg/dL (&gt;50 μmol/L)</td>
</tr>
<tr>
<td>Prothrombin Time (Seconds Prolonged), or International Normalized Ratio (INR)</td>
<td>&lt;1.7</td>
<td>4–6</td>
<td></td>
<td>&gt;6</td>
</tr>
</tbody>
</table>

<sup>a</sup> 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

<sup>b</sup> Modified total bilirubin used for patients who have Gilbert’s syndrome or who are taking indinavir or atazanavir.

### Creatinine Clearance Calculation

<table>
<thead>
<tr>
<th>Male:</th>
<th>Female:</th>
</tr>
</thead>
<tbody>
<tr>
<td>(140 – age in years) x (weight in kg)</td>
<td>(140 – age in years) x (weight in kg) x (0.85)</td>
</tr>
<tr>
<td>72 x (serum creatinine)</td>
<td>72 x (serum creatinine)</td>
</tr>
</tbody>
</table>

### Child-Pugh Classification

<table>
<thead>
<tr>
<th>Child-Pugh Classification</th>
<th>Total Child-Pugh Score&lt;sup&gt;a&lt;/sup&gt;</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>

<sup>a</sup> Sum of points for each component of the Child-Pugh Score.