



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

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## Guidelines Development Process

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

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 On some occasions, particularly when new information may affect patient safety, unpublished data presented at major conferences or prepared by the FDA and/or manufacturers as warnings to the public may be used as evidence to revise the guidelines.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

**Table 2. Rating Scheme for Recommendations**

<b>Strength of Recommendation<sup>i</sup></b>	<b>Quality of Evidence for Recommendation</b>
<b>A:</b> Strong recommendation for the statement	<b>I:</b> One or more randomized trials with clinical outcomes and/or validated laboratory endpoints
<b>B:</b> Moderate recommendation for the statement	<b>II:</b> One or more well-designed, non-randomized trials or observational cohort studies with long-term clinical outcomes
<b>C:</b> Optional recommendation for the statement	<b>III:</b> Expert opinion

**Table 3. Laboratory Testing Schedule for Monitoring Patients with HIV Before and After Initiation of Antiretroviral Therapy<sup>a</sup>** (page 1 of 3)

Laboratory Test	Timepoint or Frequency of Testing								
	Entry into Care	ART Initiation <sup>b</sup> or Modification	2 to 8 Weeks After ART Initiation or Modification	Every 3 to 6 Months	Every 6 Months	Every 12 Months	Treatment Failure	Clinically Indicated	If ART Initiation is Delayed <sup>c</sup>
HIV Serology	√ If HIV diagnosis has not been confirmed								
CD4 Count	√	√		√ During first 2 years of ART, or if viremia develops while patient is on ART, or if CD4 count is <300 cells/mm <sup>3</sup>		√ <u>After 2 Years on ART with Consistently Suppressed Viral Load:</u> CD4 Count 300–500 cells/mm <sup>3</sup> : • Every 12 months CD4 Count >500 cells/mm <sup>3</sup> : • CD4 monitoring is optional.	√	√	√ Every 3–6 months
HIV Viral Load	√	√	√ <sup>d</sup>	√ <sup>e</sup>	√ <sup>e</sup>		√	√	Repeat testing is optional.
Resistance Testing	√	√ <sup>f</sup>					√	√	√ <sup>f</sup>
HLA-B*5701 Testing		√ If considering ABC							

**Table 3. Laboratory Testing Schedule for Monitoring Patients with HIV Before and After Initiation of Antiretroviral Therapy<sup>a</sup>** (page 2 of 3)

Laboratory Test	Timepoint or Frequency of Testing								
	Entry into Care	ART Initiation <sup>b</sup> or Modification	2 to 8 Weeks After ART Initiation or Modification	Every 3 to 6 Months	Every 6 Months	Every 12 Months	Treatment Failure	Clinically Indicated	If ART Initiation is Delayed <sup>c</sup>
<b>Tropism Testing</b>		√ If considering a CCR5 antagonist					√ If considering a CCR5 antagonist, or for patients experiencing virologic failure on a CCR5 antagonist-based regimen	√	
<b>Hepatitis B Serology</b> (HBsAb, HBsAg, HBcAb total) <sup>g,h,i</sup>	√	√ May repeat if patient is nonimmune and does not have chronic HBV infection <sup>h</sup>				√ May repeat if patient is nonimmune and does not have chronic HBV infection <sup>h</sup>		√ Including prior to starting HCV DAA (see <a href="#">HCV/HIV Coinfection</a> )	
<b>Hepatitis C Screening</b> (HCV antibody or, if indicated, HCV RNA) <sup>j</sup>	√					√ Repeat HCV screening for at-risk patients <sup>k</sup>		√	
<b>Basic Chemistry<sup>l,m</sup></b>	√	√	√	√				√	√ Every 6–12 months
<b>ALT, AST, Total Bilirubin</b>	√	√	√	√				√	√ Every 6–12 months
<b>CBC with Differential</b>	√	√	√ If on ZDV	√ If on ZDV or if CD4 testing is done	√			√	√ Every 3–6 months

**Table 3. Laboratory Testing Schedule for Monitoring Patients with HIV Before and After Initiation of Antiretroviral Therapy<sup>a</sup>** (page 3 of 3)

Laboratory Test	Timepoint or Frequency of Testing								
	Entry into Care	ART Initiation <sup>b</sup> or Modification	2 to 8 Weeks After ART Initiation or Modification	Every 3 to 6 Months	Every 6 Months	Every 12 Months	Treatment Failure	Clinically Indicated	If ART Initiation is Delayed <sup>c</sup>
Fasting Lipid Profile <sup>n</sup>	√	√			√ If abnormal at last measurement	√ If normal at last measurement		√	√ If normal at baseline, annually
Fasting Glucose or Hemoglobin A1C	√	√		√ If abnormal at last measurement		√ If normal at last measurement		√	√ If normal at baseline, annually
Urinalysis <sup>m,o</sup>	√	√			√ If on TAF or TDF <sup>f</sup>	√		√	
Pregnancy Test <sup>p</sup>	√	√						√	

<sup>a</sup> This table pertains to laboratory tests done to select an ARV regimen and monitor for treatment responses or ART toxicities. Please refer to the HIV Primary Care Guidelines for guidance on other laboratory tests generally recommended for primary health care maintenance of HIV patients.<sup>1</sup>

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

<sup>c</sup> 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.

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

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

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

<sup>g</sup> 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.

<sup>h</sup> If HBsAg, HBsAb, and HBeAb test results are negative, hepatitis B vaccine series should be administered. Refer to the HIV Primary Care Guidelines and the [Adult and Adolescent Opportunistic Infections Guidelines](#) for detailed recommendations.<sup>1,2</sup>

<sup>i</sup> Most patients with isolated HBeAb have resolved HBV infection with loss of HBsAb. Consider performing an HBV viral load for confirmation. If the HBV viral load is positive, the patient may be acutely infected (and will usually display other signs of acute hepatitis) or chronically infected. If negative, the patient should be vaccinated. Refer to the HIV Primary Care Guidelines and the [Adult](#)

[and Adolescent Opportunistic Infections Guidelines](#) for more detailed recommendations.<sup>1,2</sup>

- <sup>j</sup> 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/mm<sup>3</sup>). 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.
- <sup>k</sup> 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.
- <sup>l</sup> Serum Na, K, HCO<sub>3</sub>, Cl, BUN, creatinine, glucose (preferably fasting), and creatinine-based estimated glomerular filtration rate. Serum phosphorus should be monitored in patients with chronic kidney disease who are on TAF- or TDF-containing regimens.<sup>3</sup>
- <sup>m</sup> Consult the Guidelines for the Management of Chronic Kidney Disease in HIV-Infected Patients: Recommendations of the HIV Medicine Association of the Infectious Diseases Society of America for recommendations on managing patients with renal disease.<sup>3</sup> 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).
- <sup>n</sup> Consult the National Lipid Association's recommendations for management of patients with dyslipidemia.<sup>4</sup>
- <sup>o</sup> Urine glucose and protein should be assessed before initiating TAF- or TDF-containing regimens and monitored during treatment with these regimens.
- <sup>p</sup> This applies to people of childbearing potential.

**Key to Acronyms:** 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; HBcAb = hepatitis B core antibody; HBsAb = hepatitis B surface antibody; HBsAg = hepatitis B surface antigen; HBV = hepatitis B virus; HCO<sub>3</sub> = bicarbonate; HCV = hepatitis C virus; INSTI = integrase strand transfer inhibitor; K = potassium; Na = sodium; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; ZDV = zidovudine

**Table 4. Recommendations on the Indications and Frequency of Viral Load and CD4 Count Monitoring<sup>a</sup>**

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

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

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

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



**Table 5. Recommendations for Using Drug-Resistance Assays (page 1 of 2)**

Clinical Setting and Recommendation	Rationale
<p><u>In Acute or Recent (Early) HIV Infection:</u> Drug-resistance testing is recommended <b>(AII)</b>. A genotypic assay is generally preferred <b>(AIII)</b>. Treatment should not be delayed while awaiting results of resistance testing <b>(AIII)</b>.</p>	<p>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.</p>
<p>If ART is deferred, repeat resistance testing may be considered when therapy is initiated <b>(CIII)</b>. A genotypic assay is generally preferred <b>(AIII)</b>.</p>	<p>Repeat testing when ART is initiated may be considered because the patient may have acquired a drug-resistant virus (i.e., superinfection).</p>
<p><u>In ART-Naive Patients with Chronic HIV:</u> Drug-resistance testing is recommended at entry into HIV care to guide selection of initial ART <b>(AII)</b>. A genotypic assay is generally preferred <b>(AIII)</b>.</p>	<p>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 <b>ARVs in the prescribed regimen</b>. Some drug-resistance mutations can remain detectable for years in untreated patients with chronic HIV.</p>
<p><b>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.</b></p>	<p><b>If necessary, the ART regimen can be modified once resistance test results are available.</b></p>
<p>If an INSTI is considered for an ART-naive patient <b>and/or</b> 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 <b>(AIII)</b>.</p>	<p>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.</p>
<p>If therapy is deferred, repeat resistance testing may be considered before initiation of ART <b>(CIII)</b>. A genotypic assay is generally preferred <b>(AIII)</b>.</p>	<p>Repeat testing before initiation of ART may be considered because the patient may have acquired a drug-resistant virus (i.e., a superinfection).</p> <p>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.</p>
<p>If use of a CCR5 antagonist is being considered, a co-receptor tropism assay should be performed <b>(A)</b>.</p>	<p>See <a href="#">Co-Receptor Tropism Assays</a> section.</p>
<p><u>In Patients with Virologic Failure:</u> Drug-resistance testing is recommended in patients on combination ART with HIV RNA levels &gt;1,000 copies/mL <b>(A)</b>. 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 <b>(BII)</b>.</p>	<p>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.</p>
<p>Resistance testing should be done while the patient is taking ART or, if that is not possible, within 4 weeks after ART discontinuation <b>(AII)</b>. 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 <b>(CIII)</b>.</p>	<p>The absence of detectable resistance in such patients must be interpreted with caution when designing subsequent ARV regimens, as mutations may decay with time.</p>
<p>A standard genotypic resistance assay is generally preferred for patients experiencing virologic failure on their first or second regimens <b>and for those with noncomplex resistance patterns (AII)</b>.</p>	<p>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.</p>
<p><b>All prior and current drug-resistance testing results should be reviewed and considered when designing a new regimen for a patient experiencing virologic failure (AIII).</b></p>	<p><b>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.</b></p>
<p>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 <b>(AII)</b>.</p>	<p>Genotypic assays provide information on resistance to NRTI-, NNRTI-, PI-, and INSTI-associated mutations. In some circumstances, INSTI resistance tests need to be ordered separately (clinicians should check with the testing laboratory).</p>

**Table 5. Recommendations for Using Drug-Resistance Assays (page 2 of 2)**

Clinical Setting and Recommendation	Rationale
Adding phenotypic testing to genotypic testing is generally preferred in patients with known or suspected complex drug-resistance patterns <b>(BIII)</b> .	Phenotypic testing can provide additional useful information in patients with complex drug resistance mutation patterns.
<u>In Patients with Suboptimal Suppression of Viral Load:</u> Drug-resistance testing is recommended in patients with suboptimal viral load suppression after initiation of ART <b>(AII)</b> .	Testing can determine the role of resistance <b>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.</b>
<u>In Pregnant Persons with HIV:</u> Genotypic resistance testing is recommended for all pregnant persons before initiation of ART <b>(AIII)</b> and for those entering pregnancy with detectable HIV RNA levels while on therapy <b>(AI)</b> .	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.
<u>In Patients with Undetectable Viral Load or Low-Level Viremia:</u> 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 <b>(CIII)</b> .	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** (page 1 of 2)

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.

<b>Recommended Initial Regimens for Most People with HIV</b>
Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use.
<u>INSTI plus 2 NRTIs:</u> <b>Note:</b> For individuals of childbearing potential, see Table 6b before prescribing one of these regimens. • <b>BIC/TAF/FTC (AI)</b> • DTG/ABC/3TC <sup>a</sup> (AI)—if HLA-B*5701 negative • DTG plus tenofovir <sup>b</sup> /FTC <sup>a</sup> (AI for both TAF/FTC and TDF/FTC) • RAL <sup>c</sup> plus tenofovir <sup>b</sup> /FTC <sup>a</sup> (BI for TDF/FTC, BII for TAF/FTC)
<b>Recommended Initial Regimens in Certain Clinical Situations</b>
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).
<u>INSTI plus 2 NRTIs:</u> <b>Note:</b> For individuals of childbearing potential, see Table 6b before prescribing one of these regimens. • <b>EVG/c/tenofovir<sup>b</sup>/FTC (BI for both TAF/FTC and TDF/FTC)</b> • RAL <sup>c</sup> plus ABC/3TC <sup>a</sup> (CII)—if HLA-B*5701 negative and HIV RNA <100,000 copies/mL
<u>Boosted PI plus 2 NRTIs:</u> (In general, boosted DRV is preferred over boosted ATV) • (DRV/c or DRV/r) plus tenofovir <sup>b</sup> /FTC <sup>a</sup> (AI) • (ATV/c or ATV/r) plus tenofovir <sup>b</sup> /FTC <sup>a</sup> (BI) • (DRV/c or DRV/r) plus ABC/3TC <sup>a</sup> —if HLA-B*5701 negative (BII)
<u>NNRTI plus 2 NRTIs:</u> • <b>DOR/TDF<sup>b</sup>/3TC (BI) or DOR plus TAF<sup>b</sup>/FTC (BIII)</b> • EFV plus TDF <sup>b</sup> /FTC <sup>a</sup> (BI for EFV 600 mg/TDF/FTC or EFV 600 mg/TDF/3TC, BII for EFV 600 mg plus TAF/FTC) • RPV/tenofovir <sup>b</sup> /FTC <sup>a</sup> (BI)—if HIV RNA <100,000 copies/mL and CD4 cell count >200 cells/mm <sup>3</sup>
<u>Regimens to Consider when ABC, TAF, and TDF Cannot be Used or Are Not Optimal:</u> • <b>DTG plus 3TC (BI)</b> • DRV/r plus RAL BID (CI)—if HIV RNA <100,000 copies/mL and CD4 cell count >200 cells/mm <sup>3</sup> • <b>DRV/r once daily plus 3TC<sup>a</sup> (CI)</b>
<b>Rating of Recommendations:</b> A = Strong; B = Moderate; C = Optional <b>Rating of Evidence:</b> 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

**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/ABC/3TC, EFV 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.**

<sup>a</sup> 3TC may be substituted for FTC, or vice versa. **ABC/3TC, TDF/3TC, TDF/FTC, and TAF/FTC are available as coformulated, two-NRTI tablets, and they are also available as part of various STRs. Cost, access, and availability of STR formulations are among the factors to consider when choosing between 3TC and FTC.**

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

<sup>c</sup> RAL can be given as RAL 400 mg BID or RAL 1200 mg (two, 600-mg tablets) once daily.

## Table 6a. Recommended Antiretroviral Regimens for Initial Therapy (page 2 of 2)

**Key to Acronyms:** 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; **BIC = bicitegravir**; BID = twice daily; 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; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; RAL = raltegravir; RPV = rilpivirine; **STR = single-tablet regimen**; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

## Table 6b. Considerations Before Initiating Dolutegravir and Other Integrase Strand Transfer Inhibitors as Initial Therapy

Pregnancy testing should be performed in those of childbearing potential prior to initiation of ART (**AIII**). Preliminary data suggest that there is an increased risk of NTDs in infants born to women who were receiving DTG at the time of conception.<sup>6,7</sup>

### Before Initiating DTG:

- Providers and people of childbearing potential should discuss the benefits and risks of using DTG, including the possible risk of NTDs; appropriate counseling should be provided so that the individual can make an informed decision about the use of this drug (**AIII**).
- DTG should not be prescribed for individuals:
  - Who are pregnant and within 12 weeks post-conception (**AII**); or
  - Who are of childbearing potential and planning to become pregnant (**AII**); or
  - Who are of childbearing potential, sexually active, and not using effective contraception (**AIII**).
- For those who are using effective contraception, a DTG-based regimen can be considered after weighing the risks and benefits of DTG use with the individual (**BIII**).
- It is not yet known whether other INSTIs pose a similar risk of NTDs (i.e., a class effect).
- The chemical structure of BIC is similar to DTG. There are no safety data on the use of BIC around the time of conception. For those who are of childbearing potential, but who are not pregnant, an approach similar to that outlined for DTG should be discussed before considering the use of BIC-containing ART (**AIII**).
- In a person who is pregnant, BIC is **not recommended** because of insufficient safety data (**AIII**).
- In a person who is pregnant, EVG/c is **also not recommended** because low EVG concentrations have been reported when this drug is given during the second and third trimesters (**AII**).<sup>13</sup>
- Among those who received RAL during pregnancy, the rate of fetal malformations is within the expected range for pregnancy outcomes in the United States; however, data on RAL use during the first trimester is limited to fewer than 300 deliveries. As it is currently not known whether the association between DTG and NTDs represents a class effect, this potential risk should be discussed with people of childbearing potential who prefer an INSTI-containing regimen.

**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 to Acronyms:** ART = antiretroviral therapy; BIC = bicitegravir; DTG = dolutegravir; EVG/c = elvitegravir/cobicistat; INSTI = integrase strand transfer inhibitor; NTD = neural tube defect; RAL = raltegravir

**Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios**  
(page 1 of 4)

This table provides guidance to 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.

**Note:** Preliminary data suggest that there may be an increased risk of NTDs in infants born to those who were receiving DTG at the time of conception.<sup>6,7</sup> Until more information is available, clinicians should review Table 6b for further guidance before prescribing an INSTI to a person of childbearing potential.

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
Pre-ART Characteristics	CD4 cell count <200 cells/mm <sup>3</sup>	<b>Do Not Use the Following Regimens:</b> • RPV-based regimens • DRV/r plus RAL	A higher rate of virologic failure has been observed in those with low pretreatment CD4 cell counts.
	HIV RNA >100,000 copies/mL	<b>Do Not Use the Following Regimens:</b> • RPV-based regimens • ABC/3TC with EFV or ATV/r • DRV/r plus RAL	Higher rates of virologic failure have been observed in those with high pretreatment HIV RNA levels.
	HLA-B*5701 positive or result unknown	<b>Do not use ABC-containing regimens.</b>	ABC hypersensitivity, a potentially fatal reaction, is highly associated with the presence of the HLA-B*5701 allele.
	ARV should be started before HIV drug resistance results are available (e.g., in a person with acute HIV) or when rapid initiation of ART is warranted	<b>Avoid NNRTI-based regimens.</b> <b>Avoid ABC.</b> <u>Recommended ART Regimens:</u> • (DRV/r or DRV/c) plus tenofovir <sup>a</sup> /FTC • DTG plus tenofovir <sup>a</sup> /FTC	Transmitted mutations conferring NNRTI resistance are more likely than mutations associated with PI or INSTI resistance. <b>HLA-B*5701 results may not be available rapidly.</b> <b>Transmitted resistance to DRV and DTG is rare, and these drugs have high barriers to resistance.</b> <b>Refer to Table 6b for further guidance before initiating DTG in persons of childbearing potential.</b>
ART-Specific Characteristics	A 1-pill, once-daily regimen is desired	<u>STR Options as Initial ART Include:</u> • <b>BIC/TAF/3TC</b> • <b>DOR/TDF/3TC</b> • <b>DRV/c/TAF/FTC</b> • DTG/ABC/3TC • EFV/TDF/FTC • EFV/TDF/3TC • EVG/c/TAF/FTC • EVG/c/TDF/FTC • RPV/TAF/FTC • RPV/TDF/FTC	Do not use RPV-based regimens if HIV RNA is >100,000 copies/mL and CD4 cell count is <200/mm <sup>3</sup> . Do not use DTG/ABC/3TC if patient is HLA-B*5701 positive. <b>Refer to Table 6b for further guidance before initiating an INSTI in persons of childbearing potential.</b> See <a href="#">Appendix B, Table 8</a> for ARV dose recommendations in the setting of renal impairment.
	Food effects	<u>Regimens that Can be Taken Without Regard to Food:</u> • <b>BIC-</b> , <b>DOR-</b> , DTG-, or RAL-based regimens	Oral bioavailability of these regimens is not significantly affected by food. <b>Refer to Table 6b for further guidance before initiating an INSTI in persons of childbearing potential.</b>

**Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios** (page 2 of 4)

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
ART-Specific Characteristics, continued	Food effects, continued	<p><u>Regimens that Should be Taken with Food:</u></p> <ul style="list-style-type: none"> <li>• ATV/r- or ATV/c-based regimens</li> <li>• DRV/r- or DRV/c-based regimens</li> <li>• EVG/c/TAF/FTC<sup>a</sup></li> <li>• EVG/c/TDF/FTC<sup>a</sup></li> <li>• RPV-based regimens</li> </ul>	Food improves absorption of these regimens. RPV-containing regimens should be taken with at least 390 calories of food.
		<p><u>Regimens that Should be Taken on an Empty Stomach:</u></p> <ul style="list-style-type: none"> <li>• EFV-based regimens</li> </ul>	Food increases EFV absorption and may increase CNS side effects.
Presence of Other Conditions	Chronic kidney disease (defined as CrCl <60 mL/min)	<p><b>Avoid TDF unless the patient has ESRD.</b> Use ABC or TAF.</p> <p>ABC may be used if patient is HLA-B*5701 negative. If HIV RNA &gt;100,000 copies/mL, do not use ABC/3TC plus (EFV or ATV/r).</p> <p>TAF may be used if CrCl &gt;30 mL/min.</p> <p>Consider avoiding ATV.</p> <p><u>ART Options When ABC, TAF or TDF Cannot be Used:</u></p> <ul style="list-style-type: none"> <li>• DTG plus 3TC</li> <li>• DRV/r plus 3TC</li> <li>• DRV/r plus RAL (if CD4 cell count &gt;200 cells/mm<sup>3</sup> and HIV RNA &lt;100,000 copies/mL)</li> </ul>	<p>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.</p> <p>An adjusted dose of TDF can be used in patients with ESRD or in those who are on hemodialysis. Refer to Appendix B, Table 8 for specific dosing recommendations.</p> <p>TAF has less impact on renal function and lower rates of proteinuria than TDF.</p> <p>ATV has been associated with chronic kidney disease in some observational studies.</p> <p>ABC has not been associated with renal dysfunction.</p> <p>Refer to Table 6b for further guidance before initiating an INSTI in persons of childbearing potential.</p>
	Liver disease with cirrhosis	Some ARVs are contraindicated or may require dosage modification in patients with Child-Pugh class B or C disease.	<p>Refer to Appendix B, Table 8 for specific dosing recommendations.</p> <p>Patients with cirrhosis should be carefully evaluated by an expert in advanced liver disease.</p>
	Osteoporosis	<p><b>Avoid TDF.</b></p> <p>Use ABC or TAF.</p> <p>ABC may be used if patient is HLA-B*5701 negative. If HIV RNA &gt;100,000 copies/mL, do not use ABC/3TC plus (EFV or ATV/r).</p>	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.
	Psychiatric illnesses	<p><b>Consider avoiding EFV- and RPV-based regimens.</b></p> <p>Patients on INSTI-based regimens who have pre-existing psychiatric conditions should be closely monitored.</p> <p>Some ARVs are contraindicated and some psychiatric medications need dose adjustments when coadministered with certain ARVs.</p>	<p>EFV and RPV can exacerbate psychiatric symptoms and may be associated with suicidality.</p> <p>INSTIs have been associated with adverse neuropsychiatric effects in some retrospective cohort studies and case series.</p> <p>See the drug-drug interaction tables (Tables 19a, 19b, and 19d) for dosing recommendations when drugs used for psychiatric illnesses are used with certain ARVs.</p>

**Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios** (page 3 of 4)

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
Presence of Other Conditions, continued	HAD	<p><b>Avoid EFV-based regimens if possible.</b></p> <p>Favor DTG- or DRV-based regimens.</p>	<p>EFV-related neuropsychiatric effects may confound assessment of ART's beneficial effects on improvement of HAD-related symptoms.</p> <p>There is a theoretical CNS penetration advantage of DTG- or DRV-based regimens.</p>
	Medication-assisted treatment for opioid dependence	<p><b>Opioid withdrawal may occur when EFV is initiated in patients who are on a stable dose of methadone.</b></p> <p><b>Clinical monitoring is recommended, as medications used to treat opioid dependence may need to be adjusted in some patients.</b></p>	<p>EFV reduces methadone concentrations and may lead to withdrawal symptoms.</p> <p><b>See the drug-drug interaction tables (Tables 19a, 19b, and 19d) for dosing recommendations.</b></p>
	High cardiac risk	<p>Consider avoiding ABC- and LPV/r -based regimens.</p> <p>If a boosted PI is the desired option, an ATV-based regimen may have advantages over a DRV-based regimen.</p> <p><b>BIC-, DOR-, DTG-, RAL-, or RPV-based regimens may be considered for those with high cardiac risk.</b></p>	<p>An increased CV risk with ABC has been observed in some studies.</p> <p>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.</p> <p><b>BIC-, DOR-, DTG-, RAL- or RPV-based regimens have more favorable lipid profiles than other regimens, although evidence on whether this improves CV outcomes is lacking.</b></p> <p><b>Refer to Table 6b for further guidance before initiating an INSTI in persons of childbearing potential.</b></p>
	Cardiac QTc interval prolongation	<p>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.</p>	<p>High EFV or RPV concentrations may cause QT prolongation.</p>
	Hyperlipidemia	<p><u>The Following ARV Drugs Have Been Associated with Dyslipidemia:</u></p> <ul style="list-style-type: none"> <li>• PI/r or PI/c</li> <li>• EFV</li> <li>• EVG/c</li> </ul> <p><b>BIC, DOR, DTG, RAL, and RPV have fewer lipid effects.</b></p>	<p>TDF has been associated with lower lipid levels than ABC or TAF.</p> <p><b>Refer to Table 6b for further guidance before initiating an INSTI in persons of childbearing potential.</b></p>
	Patients with history of poor adherence to non-ARV medications or inconsistent engagement in care	<p>Consider using regimens with a boosted PI or DTG.</p> <p><b>BIC also has a high barrier to resistance, but there is currently no data on its efficacy in this population.</b></p>	<p>These regimens have a high genetic barrier to resistance.</p> <p><b>Refer to Table 6b for further guidance before initiating an INSTI in persons of childbearing potential.</b></p>

**Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios** (page 4 of 4)

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
Presence of Other Conditions, continued	Pregnancy	<p>Until more information is available, <b>do not initiate a DTG-based regimen</b> for those who are pregnant and within 12 weeks post-conception, because preliminary data suggest that there is an increased risk of NTDs in infants born to those who were receiving DTG at the time of conception.<sup>6,7</sup></p> <p>Refer to <a href="#">Table 6b</a> and <a href="#">the Perinatal Guidelines</a> for further guidance on ARV use during pregnancy.</p>	
	Patients of childbearing potential who are planning to become pregnant or who are sexually active and not using effective contraception	<p>Until more information is available, <b>do not initiate a DTG-based regimen in these patients</b>, because preliminary data suggest that there is an increased risk of NTDs in infants born to those who were receiving DTG at the time of conception.<sup>6,7</sup></p> <p>Refer to <a href="#">Table 6b</a> for further guidance before initiating an INSTI.</p>	
Presence of Coinfections	HBV infection	<p>Use TDF or TAF, with FTC or 3TC, whenever possible.</p> <p><b>If TDF and TAF Are Contraindicated:</b></p> <ul style="list-style-type: none"> <li>For treatment of HBV, use FTC or 3TC with entecavir and a suppressive ART regimen (see <a href="#">HBV/HIV Coinfection</a>).</li> </ul>	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.
	HCV treatment required	Refer to recommendations in <a href="#">HCV/HIV Coinfection</a> , with special attention to potential interactions between ARV drugs and HCV drugs.	
	Treating TB disease with rifamycins	<p><b>TAF and BIC are not recommended with any rifamycin-containing regimen.</b></p> <p><b>If Rifampin is Used:</b></p> <ul style="list-style-type: none"> <li>The following are <b>not recommended</b>: <b>PI/c or PI/r, BIC, EVG, DOR, RPV, or TAF.</b></li> <li>EFV can be used without dose adjustment.</li> <li>If RAL is used, increase RAL dose to 800 mg BID. <b>Do not use once-daily RAL.</b></li> <li>Use DTG at 50 mg BID dose only in patients without selected INSTI mutations (refer to product label).</li> </ul>	<p>Rifamycins may significantly reduce TAF and BIC exposures.</p> <p>Rifampin is a strong inducer of CYP3A4 and UGT1A1 enzymes, causing significant decreases in concentrations of PIs, INSTIs, DOR, and RPV.</p> <p>Rifampin has a less significant effect on EFV concentration than on the concentrations of other NNRTIs, PIs, and INSTIs.</p> <p><b>Refer to Table 6b for further guidance before initiating an INSTI in persons of childbearing potential.</b></p> <p><b>See the drug-drug interaction tables (Tables 19a, 19b, 19c, 19d and 19e) and <a href="#">TB/HIV Coinfection</a> for information on ARV use with rifamycins.</b></p>

<sup>a</sup> TAF and TDF are two approved forms of tenofovir. 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 to Acronyms:** 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; **BIC= bicitegravir**; 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; 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; UGT = uridine diphosphate glucuronosyltransferase



**Table 8a. Characteristics of Dual-Nucleoside Reverse Transcriptase Inhibitor Options Recommended for Antiretroviral Therapy-Naive Patients**

	<b>ABC/3TC</b>	<b>TAF/FTC</b>	<b>TDF/FTC</b>	<b>TDF/3TC</b>
<b>Dosing Frequency</b>	Once daily	Once daily	Once daily	Once daily
<b>Available Coformulations for ART-Naive Patients</b>	<ul style="list-style-type: none"> <li>• ABC/3TC</li> <li>• DTG/ABC/3TC</li> </ul>	<ul style="list-style-type: none"> <li>• TAF 25 mg/FTC</li> <li>• BIC/TAF 25 mg/FTC</li> <li>• DRV/c/TAF 10 mg/FTC</li> <li>• EVG/c/TAF 10 mg/FTC</li> <li>• RPV/TAF 25 mg/FTC</li> </ul>	<ul style="list-style-type: none"> <li>• TDF/FTC</li> <li>• EFV/TDF/FTC</li> <li>• EVG/c/TDF/FTC</li> <li>• RPV/TDF/FTC</li> </ul>	<ul style="list-style-type: none"> <li>• TDF/3TC</li> <li>• DOR/TDF/3TC</li> <li>• EFV 600 mg/TDF/3TC</li> <li>• EFV 400 mg/TDF/3TC</li> </ul>
<b>Adverse Effects</b>	<p><b>ABC:</b></p> <ul style="list-style-type: none"> <li>• HSR to ABC is associated with the presence of HLA-B*5701 allele</li> <li>• Increase in CV events is associated with ABC use in some, but not all, cohort studies</li> </ul>	<p><b>TAF:</b></p> <ul style="list-style-type: none"> <li>• Renal insufficiency, proximal renal tubulopathy (less frequent than with TDF)</li> <li>• Decrease in BMD (less than with TDF; similar to ABC)</li> </ul>	<p><b>TDF:</b></p> <ul style="list-style-type: none"> <li>• Renal insufficiency, proximal renal tubulopathy</li> <li>• Decrease in BMD</li> <li>• Renal and bone toxicity are exacerbated by pharmacologic boosters</li> </ul>	<p><b>TDF:</b></p> <ul style="list-style-type: none"> <li>• Renal insufficiency, proximal renal tubulopathy</li> <li>• Decrease in BMD</li> <li>• Renal and bone toxicity are exacerbated by pharmacologic boosters</li> </ul>
		<b>FTC:</b> Nail pigmentation		<b>3TC:</b> No significant adverse effects
<b>Other Considerations</b>	<ul style="list-style-type: none"> <li>• Perform HLA-B*5701 testing before initiating ABC; if result is positive, do not start ABC and add ABC to allergy list</li> <li>• If HIV RNA &gt;100,000 copies/mL, use only with DTG</li> </ul>	<p>Also used for HBV treatment. Discontinuation may precipitate flare of HBV.</p> <p>See <a href="#">Appendix B, Table 8</a> for dose recommendations in patients with renal insufficiency.</p>		

**Key to Acronyms:** 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; BIC= bictegravir; 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; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

**Table 8b. Characteristics of Integrase Strand Transfer Inhibitors That Are Recommended for Antiretroviral Therapy-Naive Patients**

**Note:** Preliminary data suggest that there may be an increased risk of NTDs in infants born to those who were receiving DTG at the time of conception.<sup>6,7</sup> Until more information is available:

- Pregnancy testing should be performed for those of childbearing potential prior to initiation of ART.
- DTG is **not recommended** for ART-naive individuals:
  - Who are pregnant and within 12 weeks post-conception, *or*
  - Who are of childbearing potential and who are planning to become pregnant or who are sexually active and not using effective contraception.

Clinicians should refer to Table 6b for further guidance before initiating an INSTI.

	<b>BIC</b>	<b>DTG</b>	<b>EVG</b>	<b>RAL</b>
<b>Dosing Frequency</b>	Once daily	<u>Once Daily:</u> • In ART-naive or INSTI-naive persons  <u>Twice Daily:</u> • If used with certain CYP3A4 and UGT1A1 inducers; <i>or</i> • In INSTI-experienced persons with certain INSTI DRMs	Once daily; requires boosting with COBI	• 400 mg BID, <i>or</i> • 1200 mg (two 600-mg tablets) once daily
<b>STR Available for ART-Naive Patients</b>	BIC/TAF/FTC	DTG/ABC/3TC	• EVG/c/TAF/FTC • EVG/c/TDF/FTC	No
<b>Available as a Single-Drug Tablet</b>	No	Yes	No	Yes
<b>Approved for ART-Experienced Patients</b>	No	Yes, with BID dosing for patients with some INSTI DRMs	No	Yes, for patients with DRM to PI/r or NNRTIs, but no DRM to INSTIs
<b>Virologic Efficacy Against EVG- or RAL-Resistant HIV</b>	<i>In vitro</i> data indicate activity, but no clinical trial data are available	Yes, for some isolates; effective with 50 mg BID dose	No	No
<b>Adverse Effects</b>	Nausea, diarrhea (GI disturbance greater with EVG/c), headache, insomnia. Depression and suicidality are rare, occurring primarily in patients with pre-existing psychiatric conditions.			
	↑ CPK (4%)	Hypersensitivity, hepatotoxicity, ↑ CPK, myositis	↑ TG, ↑ LDL	↑ CPK, myopathy, hypersensitivity, SJS/TEN
<b>CYP3A4 Drug-Drug Interactions</b>	CYP3A4 substrate	CYP3A4 substrate (minor)	EVG is a CYP3A4 substrate; COBI is a CYP3A4 inhibitor	No
<b>Chelation with Poly-valent Cation Supplements and Antacids</b>	Oral absorption of all INSTIs may be reduced by polyvalent cations. See <a href="#">Table 19d</a> for recommendations regarding dosing separation of INSTIs and these drugs.			
<b>Other Key Potential Drug Interactions</b>	UGT1A1 substrate, OAT1 and MATE2 inhibitor	p-gp substrate, UGT1A1 substrate	EVG is a UGT1A1 substrate; COBI is a p-gp inhibitor	UGT1A1 substrate

**Key to Acronyms:** 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; BIC = bictegravir; BID = twice daily; COBI = cobicistat; CPK = creatine phosphokinase; CYP = cytochrome P; DRM = drug resistance mutation; 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; NNRTI = non-nucleoside reverse transcriptase inhibitor; NTD = neural tube defect; OAT = organic anionic 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**

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

**Key to Acronyms:** 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**

	<b>ATV</b>	<b>DRV</b>
<b>Dosing Frequency</b>	Once daily	<ul style="list-style-type: none"> <li>• Once daily for PI-naive patients</li> <li>• Twice daily for PI-experienced patients with certain PI mutations</li> </ul>
<b>PK Boosting</b>	PK-boosting with RTV or COBI is generally recommended. Unboosted ATV is also FDA-approved for ART-naive patients.	DRV should only be used with a PK booster (i.e., RTV or COBI).
<b>Fixed-Dose Formulation</b>	• ATV/c	<ul style="list-style-type: none"> <li>• DRV/c</li> <li>• DRV/c/TAF/FTC</li> </ul>
<b>Available as a Single-Drug Tablet</b>	Yes	Yes
<b>Adverse Effects</b>	<ul style="list-style-type: none"> <li>• Jaundice</li> <li>• Indirect hyperbilirubinemia</li> <li>• Cholelithiasis</li> <li>• Nephrolithiasis</li> <li>• PR prolongation</li> </ul>	<ul style="list-style-type: none"> <li>• Skin rash</li> <li>• Increase in serum transaminases</li> <li>• Hyperlipidemia</li> <li>• A higher cardiovascular risk was reported in participants taking DRV-based regimens than in those taking ATV-based regimens in an observational cohort study.</li> </ul>
<b>CYP3A4 Drug-Drug Interactions</b>	CYP3A4 substrate, inhibitor	CYP3A4 substrate, inhibitor
<b>Other Significant Drug Interactions</b>	ATV absorption is reduced when ATV is given with acid-lowering therapies. See Table 19a for ATV dosing recommendations when the drug is coadministered with acid-lowering agents.	N/A

**Key to Acronyms:** 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; PI = protease inhibitor; PK = pharmacokinetic; RTV = ritonavir; TAF = tenofovir alafenamide

**Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy** (page 1 of 5)

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

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
Dual-NRTI	ABC/3TC	<ul style="list-style-type: none"> <li>• Coformulated with DTG</li> <li>• Generic formulations are available for ABC/3TC, ABC, and 3TC.</li> </ul>	<ul style="list-style-type: none"> <li>• May cause life-threatening HSRs in patients who test positive for the HLA-B*5701 allele. As a result, HLA-B*5701 testing is required before use.</li> <li>• In the ACTG 5202 study, patients with baseline HIV RNA <math>\geq 100,000</math> 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.</li> <li>• ABC use has been associated with CV disease and cardiac events in some, but not all, observational studies.</li> </ul>
	TAF/FTC	<ul style="list-style-type: none"> <li>• Coformulated with BIC, DRV/c, EVG/c, or RPV</li> <li>• Active against HBV; a recommended dual-NRTI option for patients with HIV/HBV coinfection</li> <li>• Smaller decline in renal function, less proteinuria, and smaller reductions in BMD than TDF/FTC</li> <li>• Approved for patients with eGFR <math>\geq 30</math> mL/min</li> </ul>	<ul style="list-style-type: none"> <li>• TDF is associated with lower lipid levels than TAF, perhaps because TDF results in higher plasma levels of tenofovir, which lowers lipids.</li> </ul>
	TDF/3TC	<ul style="list-style-type: none"> <li>• Coformulated with DOR and EFV</li> <li>• Available as the following generic formulations:                             <ul style="list-style-type: none"> <li>• TDF</li> <li>• 3TC</li> <li>• TDF/3TC</li> <li>• EFV/TDF/3TC</li> </ul> </li> <li>• Long-term clinical experience</li> <li>• Active against HBV</li> </ul>	<ul style="list-style-type: none"> <li>• Renal toxicity, including proximal tubulopathy and acute or chronic renal insufficiency, especially when combined with pharmacologic boosters.</li> <li>• Osteomalacia has been reported as a consequence of proximal tubulopathy.</li> <li>• Decreased BMD has been associated with use of TDF, especially when combined with pharmacologic boosters.</li> </ul>
	TDF/FTC	<ul style="list-style-type: none"> <li>• Coformulated with EFV, EVG/c, and RPV as STRs</li> <li>• Active against HBV; a recommended dual-NRTI option for patients with HIV/HBV coinfection</li> <li>• Better virologic responses than ABC/3TC in patients with baseline viral loads <math>\geq 100,000</math> copies/mL when combined with ATV/r or EFV</li> <li>• Associated with lower lipid levels than ABC or TAF</li> </ul>	<ul style="list-style-type: none"> <li>• Renal toxicity, including proximal tubulopathy and acute or chronic renal insufficiency, especially when combined with pharmacologic boosters.</li> <li>• Osteomalacia has been reported as a consequence of proximal tubulopathy.</li> <li>• Decreased BMD has been associated with use of TDF, especially when combined with pharmacologic boosters.</li> </ul>

**Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy (page 2 of 5)**

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
INSTI	<b>BIC</b>	<ul style="list-style-type: none"> <li>• Coformulated with TAF/FTC</li> <li>• In trials in ART-naïve participants, BIC resistance was not detected</li> <li>• No food requirement</li> </ul>	<ul style="list-style-type: none"> <li>• Compared to other INSTIs, BIC has the shortest post-marketing experience.</li> <li>• 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 <a href="#">Table 19d</a>.</li> <li>• Inhibits tubular secretion of creatinine without affecting glomerular function.</li> <li>• CYP3A4 and UGT1A1 substrate (but not a CYP3A4 inducer or inhibitor); potential for drug interactions.</li> </ul>
	<b>DTG</b>	<ul style="list-style-type: none"> <li>• Higher barrier to resistance than EVG or RAL</li> <li>• Coformulated with ABC and 3TC</li> <li>• No food requirement</li> <li>• No CYP3A4 interactions</li> <li>• Favorable lipid profile</li> </ul>	<ul style="list-style-type: none"> <li>• Preliminary data suggests that DTG use before pregnancy and through conception may be associated with an increased risk of NTDs in the infant. See text and <a href="#">Table 6b</a> for recommendations.</li> <li>• 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 <a href="#">Table 19d</a>.</li> <li>• Inhibits renal tubular secretion of Cr and can increase serum Cr without affecting glomerular function.</li> <li>• UGT1A1 substrate; potential for drug interactions (see <a href="#">Table 19d</a>).</li> <li>• Depression and suicidal ideation (rare; usually in patients with pre-existing psychiatric conditions).</li> </ul>
	<b>EVG/c</b>	<ul style="list-style-type: none"> <li>• Coformulated with TDF/FTC or TAF/FTC</li> <li>• Compared with ATV/r, causes smaller increases in total and LDL cholesterol</li> </ul>	<ul style="list-style-type: none"> <li>• EVG/c/TDF/FTC is only recommended for patients with baseline CrCl <math>\geq 70</math> mL/min; this regimen should be discontinued if CrCl decreases to <math>&lt; 50</math> mL/min.</li> <li>• COBI is a potent CYP3A4 inhibitor, which can result in significant interactions with CYP3A substrates.</li> <li>• 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 <a href="#">Table 19d</a>.</li> <li>• COBI inhibits active tubular secretion of Cr and can increase serum Cr without affecting renal glomerular function.</li> <li>• Has a lower barrier to resistance than boosted PI-, <b>BIC</b>-, or DTG-based regimens.</li> <li>• Food requirement.</li> <li>• Depression and suicidal ideation (rare; usually in patients with pre-existing psychiatric conditions).</li> </ul>

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

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
INSTI, continued	RAL	<ul style="list-style-type: none"> <li>• Compared to other INSTIs, has longest post-marketing experience</li> <li>• No food requirement</li> <li>• No CYP3A4 interactions</li> <li>• Favorable lipid profile</li> </ul>	<ul style="list-style-type: none"> <li>• Has a lower barrier to resistance than boosted PI-, <b>BIC-</b>, or DTG-based regimens.</li> <li>• Increases in creatine kinase, myopathy, and rhabdomyolysis have been reported.</li> <li>• Rare cases of severe HSRs (including SJS and TEN) have been reported.</li> <li>• Higher pill burden than other INSTI-based regimens.</li> <li>• No STR formulation.</li> <li>• 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 <a href="#">Table 19d</a>.</li> <li>• UGT1A1 substrate; potential for drug interactions (see <a href="#">Table 19d</a>).</li> <li>• Depression and suicidal ideation (rare; usually in patients with pre-existing psychiatric conditions).</li> </ul>
NNRTI	DOR	<ul style="list-style-type: none"> <li>• Coformulated with TDF/3TC</li> <li>• Compared to EFV, CNS side effects are less frequent</li> <li>• No food requirement</li> <li>• Favorable lipid profile</li> </ul>	<ul style="list-style-type: none"> <li>• Shorter-term clinical experience than with EFV and RPV.</li> <li>• Potential for CYP450 drug interactions (see Tables <a href="#">19b</a>, <a href="#">20a</a> and <a href="#">20b</a>).</li> <li>• Treatment-emergent DOR resistance mutations may confer resistance to certain NNRTIs.</li> </ul>
	EFV	<ul style="list-style-type: none"> <li>• <b>EFV 600 mg is</b> coformulated with TDF/FTC <b>and TDF/3TC</b></li> <li>• <b>EFV 400 mg is</b> coformulated with TDF/3TC</li> <li>• <b>EFV 600-mg dose</b> has long-term clinical experience <b>and</b> EFV-based regimens (except for EFV plus ABC/3TC) have well-documented efficacy in patients with high HIV RNA</li> </ul>	<ul style="list-style-type: none"> <li>• Short- and long-term neuropsychiatric (CNS) side effects, including depression and, in some studies, suicidality and catatonia. <b>Screening for depression and suicidality is recommended in people with HIV who are taking a regimen that includes EFV.</b></li> <li>• Teratogenic in nonhuman primates, although no rate increase has been seen in humans.</li> <li>• Dyslipidemia</li> <li>• Rash</li> <li>• 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.</li> <li>• Transmitted resistance is more common than with PIs and INSTIs.</li> <li>• Greater risk of resistance at the time of treatment failure than with PIs.</li> <li>• Potential for CYP450 drug interactions (see Tables <a href="#">19b</a> and <a href="#">20a</a>).</li> <li>• Should be taken on an empty stomach (food increases drug absorption and CNS toxicities).</li> </ul>

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

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
NNRTI, continued	RPV	<ul style="list-style-type: none"> <li>• Coformulated with TDF/FTC and TAF/FTC</li> <li>• RPV/TDF/FTC and RPV/TAF/FTC have smaller pill sizes than other coformulated ARV drugs</li> <li>• Compared with EFV:               <ul style="list-style-type: none"> <li>• Fewer CNS adverse effects</li> <li>• Fewer lipid effects</li> <li>• Fewer rashes</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <b>Not recommended</b> in patients with pre-ART HIV RNA &gt;100,000 copies/mL or CD4 cell counts &lt;200 cells/mm<sup>3</sup> because of higher rate of virologic failure in these patients.</li> <li>• Depression and suicidality</li> <li>• 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.</li> <li>• Rash</li> <li>• Transmitted resistance is more common than with PIs and INSTIs.</li> <li>• More NNRTI-, TDF-, and 3TC-associated mutations at virologic failure than with regimens that contain EFV and 2 NRTIs.</li> <li>• Potential for CYP450 drug interactions (see <a href="#">Tables 19b</a> and <a href="#">20a</a>).</li> <li>• Meal requirement (&gt;390 kcal)</li> <li>• Requires acid for adequate absorption.               <ul style="list-style-type: none"> <li>• <b>Contraindicated</b> with PPIs.</li> <li>• Use with H2 antagonists or antacids with caution (see <a href="#">Table 19a</a> for detailed dosing information).</li> </ul> </li> </ul>
PIs	ATV/c or ATV/r	<ul style="list-style-type: none"> <li>• Higher barrier to resistance than NNRTIs, EVG, and RAL</li> <li>• PI resistance at the time of treatment failure is uncommon with PK-enhanced PIs</li> <li>• ATV/c and ATV/r have similar virologic activity and toxicity profiles</li> <li>• 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.</li> <li>• <b>Individual ATV and RTV components available as generics</b></li> </ul>	<ul style="list-style-type: none"> <li>• Commonly causes indirect hyperbilirubinemia, which may manifest as scleral icterus or jaundice.</li> <li>• Food requirement</li> <li>• Absorption depends on food and low gastric pH (see <a href="#">Table 19a</a> for interactions with H2 antagonists, antacids, and PPIs).</li> <li>• Nephrolithiasis, cholelithiasis, nephrotoxicity</li> <li>• GI adverse effects</li> <li>• CYP3A4 inhibitors and substrates: potential for drug interactions (see <a href="#">Table 19a</a>).</li> </ul>
	ATV/c (Specific considerations)	<ul style="list-style-type: none"> <li>• Coformulated tablet</li> </ul>	<ul style="list-style-type: none"> <li>• COBI inhibits active tubular secretion of Cr and can increase serum Cr without affecting renal glomerular function.</li> <li>• Coadministration with TDF <b>is not recommended</b> in patients with CrCl &lt;70 mL/min.</li> <li>• COBI (like RTV) is a potent CYP3A4 inhibitor, which can result in significant interactions with CYP3A substrates.</li> </ul>
	DRV/c or DRV/r	<ul style="list-style-type: none"> <li>• Higher barrier to resistance than NNRTIs, EVG, and RAL</li> <li>• PI resistance at the time of treatment failure is uncommon with PK-enhanced PIs</li> </ul>	<ul style="list-style-type: none"> <li>• Skin rash</li> <li>• Food requirement</li> <li>• GI adverse effects</li> <li>• CYP3A4 inhibitors and substrates: potential for drug interactions (see <a href="#">Table 19a</a>).</li> <li>• Increased CV risk reported in one observational cohort study.</li> </ul>



**Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy** (page 5 of 5)

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
PIs, continued	DRV/c (Specific considerations)	<ul style="list-style-type: none"> <li>• Coformulated as DRV/c <b>and DRV/c/TAF/FTC</b></li> </ul>	<ul style="list-style-type: none"> <li>• COBI inhibits active tubular secretion of Cr and can increase serum Cr without affecting renal glomerular function.</li> <li>• Coadministration with TDF <b>is not recommended</b> in patients with CrCl &lt;70 mL/min.</li> <li>• COBI (like RTV) is a potent CYP3A4 inhibitor, which can result in significant interactions with CYP3A substrates.</li> </ul>
	LPV/r	<ul style="list-style-type: none"> <li>• Only RTV-coformulated PI</li> <li>• No food requirement</li> </ul>	<ul style="list-style-type: none"> <li>• Requires RTV 200 mg per day.</li> <li>• Possible higher risk of MI associated with cumulative use of LPV/r.</li> <li>• PR and QT interval prolongation have been reported. Use with caution in patients at risk of cardiac conduction abnormalities or in patients receiving other drugs with similar effects.</li> <li>• Possible nephrotoxicity</li> <li>• CYP3A4 inhibitors and substrates: potential for drug interactions (see <a href="#">Table 19a</a>).</li> </ul>

**Key to Acronyms:** 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; eGFR = estimated glomerular filtration rate; EFV = efavirenz; 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 = lopinavir; 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 (page 1 of 3)**

ARV Components or Regimens	Reasons for <u>Not</u> Recommending as Initial Therapy
<b>NRTIs</b>	
<b>ABC/3TC/ZDV (Coformulated)</b> As triple-NRTI combination regimen	<ul style="list-style-type: none"> <li>• Inferior virologic efficacy</li> </ul>
<b>ABC/3TC/ZDV plus TDF</b> As quadruple-NRTI combination regimen	<ul style="list-style-type: none"> <li>• Inferior virologic efficacy</li> </ul>
<b>d4T plus 3TC</b>	<ul style="list-style-type: none"> <li>• Significant toxicities (including lipodystrophy, peripheral neuropathy) and hyperlactatemia (including symptomatic and life-threatening lactic acidosis, hepatic steatosis, and pancreatitis)</li> </ul>
<b>ddl plus 3TC (or FTC)</b>	<ul style="list-style-type: none"> <li>• Inferior virologic efficacy</li> <li>• Limited clinical trial experience in ART-naive patients</li> <li>• ddl toxicities, such as pancreatitis and peripheral neuropathy</li> </ul>
<b>ddl plus TDF</b>	<ul style="list-style-type: none"> <li>• High rate of early virologic failure</li> <li>• Rapid selection of resistance mutations</li> <li>• Potential for immunologic nonresponse/CD4 cell decline</li> <li>• Increased ddl drug exposure and toxicities</li> </ul>

**Table 10. Antiretroviral Components or Regimens Not Recommended as Initial Therapy (page 2 of 3)**

ARV Components or Regimens	Reasons for <u>Not</u> Recommending as Initial Therapy
<b>NRTIs, continued</b>	
<b>ZDV/3TC</b>	<ul style="list-style-type: none"> <li>• 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</li> </ul>
<b>NNRTIs</b>	
<b>DLV</b>	<ul style="list-style-type: none"> <li>• Inferior virologic efficacy</li> <li>• Inconvenient (three times daily) dosing</li> </ul>
<b>ETR</b>	<ul style="list-style-type: none"> <li>• Insufficient data in ART-naive patients</li> </ul>
<b>NVP</b>	<ul style="list-style-type: none"> <li>• Associated with serious and potentially fatal toxicity (hepatic events and severe rash, including SJS and TEN)</li> <li>• When compared to EFV, NVP did not meet noninferiority criteria</li> </ul>
<b>PIs</b>	
<b>ATV (Unboosted)</b>	<ul style="list-style-type: none"> <li>• Less potent than boosted ATV</li> </ul>
<b>DRV (Unboosted)</b>	<ul style="list-style-type: none"> <li>• Use without RTV or COBI has not been studied</li> </ul>
<b>FPV (Unboosted)</b> or <b>FPV/r</b>	<ul style="list-style-type: none"> <li>• Virologic failure with unboosted FPV-based regimen may result in selection of mutations that confer resistance to FPV and DRV</li> <li>• Less clinical trial data for FPV/r than for other RTV-boosted PIs</li> </ul>
<b>IDV (Unboosted)</b>	<ul style="list-style-type: none"> <li>• Inconvenient dosing (3 times daily with meal restrictions)</li> <li>• Fluid requirement</li> <li>• IDV toxicities, such as nephrolithiasis and crystalluria</li> </ul>
<b>IDV/r</b>	<ul style="list-style-type: none"> <li>• Fluid requirement</li> <li>• IDV toxicities, such as nephrolithiasis and crystalluria</li> </ul>
<b>LPV/r</b>	<ul style="list-style-type: none"> <li>• Higher pill burden than other PI-based regimens</li> <li>• Higher RTV dose than other PI-based regimens</li> <li>• GI intolerance</li> </ul>
<b>NFV</b>	<ul style="list-style-type: none"> <li>• Inferior virologic efficacy</li> <li>• Diarrhea</li> </ul>
<b>RTV as sole PI</b>	<ul style="list-style-type: none"> <li>• High pill burden</li> <li>• GI intolerance</li> <li>• Metabolic toxicity</li> </ul>
<b>SQV (Unboosted)</b>	<ul style="list-style-type: none"> <li>• Inadequate bioavailability</li> <li>• Inferior virologic efficacy</li> </ul>
<b>SQV/r</b>	<ul style="list-style-type: none"> <li>• High pill burden</li> <li>• Can cause QT and PR prolongation; requires pretreatment and follow-up ECG</li> </ul>
<b>TPV/r</b>	<ul style="list-style-type: none"> <li>• Inferior virologic efficacy</li> <li>• Higher rate of adverse events than other RTV-boosted PIs</li> <li>• Higher dose of RTV required for boosting than other RTV-boosted PIs</li> </ul>
<b>Entry Inhibitors</b>	
<b>T-20</b> Fusion Inhibitor	<ul style="list-style-type: none"> <li>• Only studied in patients with virologic failure</li> <li>• Twice-daily subcutaneous injections</li> <li>• High rate of injection site reactions</li> </ul>
<b>IBA</b> CD4 Post-Attachment Inhibitor	<ul style="list-style-type: none"> <li>• Only studied in a very small number of patients with virologic failure</li> <li>• Requires IV therapy</li> <li>• High cost</li> </ul>

**Table 10. Antiretroviral Components or Regimens Not Recommended as Initial Therapy (page 3 of 3)**

ARV Components or Regimens	Reasons for <u>Not</u> Recommending as Initial Therapy
<b>Entry Inhibitors</b> , continued	
<b>MVC</b> CCR5 Antagonist	<ul style="list-style-type: none"> <li>• Requires testing for CCR5 tropism before initiation of therapy</li> <li>• No virologic benefit when compared with other recommended regimens</li> <li>• Requires twice-daily dosing</li> </ul>

**Key to Acronyms:** 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 = nelfinavir; 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 with 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.

Preliminary data from Botswana suggested that there is an increased risk of NTDs in infants born to individuals who were receiving DTG at the time of conception.<sup>47,48</sup> Pregnancy testing should therefore be performed for those of childbearing potential prior to initiation of DTG. If there is an alternative option, DTG should not be prescribed for those who are pregnant and within 12 weeks post-conception or those who are of childbearing potential and who are planning to become pregnant or who are not using effective contraception. When DTG is the only treatment option, or one of few treatment options, providers should counsel individuals who are pregnant or of childbearing potential about the possible association between NTDs and DTG use during conception. The decision of whether to initiate or continue DTG should be made after careful consideration of this risk and the risks of persistent viremia in the patient and HIV transmission to the fetus if pregnancy occurs while the patient is not on effective ART.

Clinical Scenario	Type of Failing Regimen	Resistance Considerations	New Regimen Options <sup>a,b</sup>	Goal
First Regimen Failure	NNRTI plus 2 NRTIs	Most likely resistant to NNRTI +/- 3TC/FTC (i.e., NNRTI mutations +/- M184V/I). <sup>c</sup> Additional NRTI mutations may also be present.	<ul style="list-style-type: none"> <li>• Boosted PI plus 2 NRTIs (at least 1 active) <b>(AIII)</b>; or</li> <li>• DTG<sup>d</sup> plus 2 NRTIs (at least 1 active) <b>(AI)</b>; or</li> <li>• Boosted PI plus INSTI <b>(AIII)</b></li> </ul>	Resuppression
	Boosted PI plus 2 NRTIs	Most likely no resistance, or resistance only to 3TC/FTC (i.e., M184V/I, without resistance to other NRTIs) <sup>c</sup>	<ul style="list-style-type: none"> <li>• Continue same regimen <b>(AII)</b>; or</li> <li>• Another boosted PI plus 2 NRTIs (at least 1 active) <b>(AII)</b>; or</li> <li>• INSTI plus 2 NRTIs (at least 1 active; if only 1 of the NRTIs is fully active, or, if adherence is a concern, DTG<sup>d</sup> is preferred over the other INSTIs) <b>(AIII)</b>; or</li> <li>• Another boosted PI plus INSTI <b>(BIII)</b></li> </ul>	Resuppression
	INSTI plus 2 NRTIs	No INSTI resistance (can have 3TC/FTC resistance, i.e., only M184V/I, usually without resistance to other NRTIs) <sup>c</sup>	<ul style="list-style-type: none"> <li>• Boosted PI plus 2 NRTIs (at least 1 active) <b>(AIII)</b>; or</li> <li>• DTG<sup>d</sup> plus 2 NRTIs (at least 1 active) <b>(AIII)</b>; or</li> <li>• Boosted PI plus INSTI <b>(BIII)</b></li> </ul>	Resuppression

**Table 11. Antiretroviral Options for Patients with Virologic Failure**

Clinical Scenario	Type of Failing Regimen	Resistance Considerations	New Regimen Options <sup>a,b</sup>	Goal
First Regimen Failure, continued	INSTI plus 2 NRTIs	EVG or RAL +/- 3TC/FTC resistance  Resistance to first-line BIC or DTG is rare	<ul style="list-style-type: none"> <li>• Boosted PI plus 2 NRTIs (at least 1 active) <b>(AIII)</b>; <i>or</i></li> <li>• DTG<sup>d,e</sup> twice daily (if patient is sensitive to DTG) plus 2 active NRTIs <b>(AIII)</b>; <i>or</i></li> <li>• DTG<sup>d,e</sup> twice daily (if patient is sensitive to DTG) plus a boosted PI <b>(AIII)</b></li> <li>• <b>BIC has not been studied in this setting and cannot be recommended.</b></li> </ul>	Resuppression
Second Regimen Failure and Beyond	Drug resistance with active treatment options	Use past and current genotypic +/- phenotypic resistance testing and ART history in designing new regimen	<ul style="list-style-type: none"> <li>• At least 2, and preferably 3, fully active agents <b>(AI)</b></li> <li>• Partially active drugs may be used when no other options are available</li> <li>• Consider using an ARV with a different mechanism of action</li> </ul>	Resuppression
	Multiple or extensive drug resistance with few treatment options	Use past and current genotypic and phenotypic resistance testing to guide therapy  Consider viral tropism assay if use of MVC is considered  Consult an expert in drug resistance, if needed	<ul style="list-style-type: none"> <li>• Identify as many active or partially active drugs as possible based on resistance test results</li> <li>• Consider using an ARV with a different mechanism of action</li> <li>• Consider enrollment into clinical trials or expanded access programs for investigational agents, if available</li> <li>• Discontinuation of ARVs <b>is not recommended.</b></li> </ul>	Resuppression, if possible; otherwise, keeping viral load as low as possible and CD4 cell count as high as possible
Previously on Treatment, Suspected Drug Resistance, Limited or Incomplete ART and Resistance History	Unknown	Obtain medical records if possible  Resistance testing may be helpful in identifying drug resistance mutations, even if the patient has been off ART. Keep in mind that resistance mutations may not be detected in the absence of drug pressure.	<ul style="list-style-type: none"> <li>• Consider restarting the old regimen, and obtain viral load and resistance testing 2–4 weeks after reintroduction of therapy</li> <li>• If there is no available ARV history, consider initiating a regimen with drugs with high genetic barriers to resistance (e.g., DTG<sup>d,e</sup> and/or boosted DRV)</li> </ul>	Resuppression

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

<sup>b</sup> When switching an ARV regimen in a patient with HIV/HBV 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> Preliminary data from Botswana suggested that there is an increased risk of NTDs in infants born to those who were receiving DTG at the time of conception.<sup>47,48</sup> Pregnancy testing should therefore be performed for those of childbearing potential prior to initiation of DTG. Please refer to the discussion at the beginning of this table for further recommendations.

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

**Key to Acronyms:** 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

**Table 12. Identifying, Diagnosing, and Treating Acute and Recent HIV-1 Infection**

<p><u>Suspicion of Acute HIV-1 Infection:</u></p> <ul style="list-style-type: none"><li>• Health care providers should consider the possibility of acute HIV-1 infection in individuals with signs, symptoms, or the laboratory findings described below and recent (within 2 to 6 weeks) high risk of exposure to HIV-1.<sup>a</sup><ul style="list-style-type: none"><li>• Signs, symptoms, or laboratory findings of acute HIV-1 infection may include but are not limited to one or more of the following: fever, lymphadenopathy, skin rash, myalgia, arthralgia, headache, diarrhea, oral ulcers, leucopenia, thrombocytopenia, and transaminase elevation.</li><li>• High-risk exposures include sexual contact with a person who has HIV-1 infection or a person at risk of HIV-1 infection, sharing of injection drug use paraphernalia, or any exposure in which an individual's mucous membranes or breaks in the skin come in contact with bodily fluid that potentially carries HIV-1.</li></ul></li><li>• <b>Differential Diagnosis:</b> The differential diagnosis of HIV-1 infection may include but is not limited to viral illnesses such as EBV and non-EBV (e.g., cytomegalovirus) infectious mononucleosis syndromes, influenza, viral hepatitis, streptococcal infection, or syphilis.</li></ul> <p><u>Evaluation/Diagnosis of Acute HIV-1 Infection:</u></p> <ul style="list-style-type: none"><li>• Acute HIV-1 infection is defined as detectable HIV-1 RNA or p24 antigen (the antigen used in currently available HIV Ag/Ab combination assays) in the setting of a negative or indeterminate HIV-1 antibody test result.</li><li>• A reactive HIV antibody test result or Ag/Ab combination test result must be followed by supplemental confirmatory testing.</li><li>• A negative or indeterminate HIV-1 antibody test result in a person with a reactive Ag/Ab test result or in whom acute HIV-1 infection is suspected requires plasma HIV-1 RNA testing to diagnose acute HIV-1 infection.</li><li>• A positive result on a quantitative or qualitative plasma HIV-1 RNA test in the setting of a negative or indeterminate antibody test result indicates that acute HIV-1 infection is highly likely. In this case, the diagnosis of HIV-1 infection should be later confirmed by subsequent documentation of HIV-1 antibody seroconversion.</li></ul> <p><u>Antiretroviral Therapy After Diagnosis of Early HIV-1 Infection:</u></p> <ul style="list-style-type: none"><li>• ART is recommended for all individuals with HIV-1 (<b>AI</b>) and should be offered to all patients with early HIV-1 infection.</li><li>• <b>A pregnancy test should be performed for all individuals who receive a diagnosis of early HIV infection and who are of childbearing potential (AIII).</b></li><li>• Pregnant patients with early HIV-1 infection should begin ART as soon as possible for their own health and to prevent perinatal transmission of HIV-1 (<b>AI</b>).</li><li>• A blood sample for genotypic drug resistance testing should be obtained before initiation of ART to guide the selection of the regimen (<b>AII</b>), but ART should be initiated as soon as possible, often prior to availability of resistance test results. If resistance is subsequently identified, treatment should be modified appropriately.</li><li>• If no resistance data are available, then a pharmacologically boosted PI-based regimen is recommended, because resistance to PIs emerges slowly and clinically significant transmitted resistance to PIs is uncommon. Boosted DRV (DRV/r or DRV/c) plus FTC and either TDF or TAF is a recommended regimen in this setting (<b>AIII</b>). For similar reasons, DTG plus FTC and either TDF or TAF are reasonable options, although the data regarding transmission of INSTI-resistant HIV and the efficacy of this regimen in early HIV infection are limited (<b>AIII</b>).</li><li>• <b>Preliminary data from Botswana suggested that infants born to women who were receiving DTG at the time of conception have an increased risk of neural tube defects. Until more information is available, DTG should not be prescribed for individuals:</b><ul style="list-style-type: none"><li>• <b>Who are pregnant and within 12 weeks post-conception (AII);</b></li><li>• <b>Who are of childbearing potential, who are sexually active, and who are not using effective contraception (AII); or</b></li><li>• <b>Who are contemplating pregnancy (AII).</b></li></ul></li><li>• In patients without transmitted drug-resistant virus, ART should be initiated with one of the combination regimens recommended for patients with chronic HIV-1 infection (see <a href="#">What to Start</a>) (<b>AIII</b>).</li><li>• Once initiated, the goal of ART should be sustained plasma virologic suppression, and ART should be continued indefinitely (<b>AIII</b>).</li></ul>
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<sup>a</sup> In some settings, behaviors that increase the risk of HIV-1 infection may not be recognized or perceived as risky by the health care provider or the patient, or both. Thus, even in the absence of reported high-risk behaviors, symptoms and signs consistent with acute retroviral syndrome should motivate practitioners to consider a diagnosis of acute HIV-1 infection.

**Key to Acronyms:** Ag/Ab = antigen/antibody; ART = antiretroviral therapy; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EBV = Epstein-Barr virus; FTC = emtricitabine; INSTI = integrase strand transfer inhibitor; PI = protease inhibitor; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

**Table 13. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of HCV in Adults with HIV** (page 1 of 4)

The recommendations in this table for concomitant use of selected HIV drugs with FDA-approved HCV DAA drugs are based on available PK interaction data or are predictions based on the known metabolic pathway of the agents. In some cases, there are not enough data to make any recommendations, and these instances are indicated in the table. In all cases where HIV and HCV drugs are used concomitantly, patients should be closely monitored for HIV and HCV virologic efficacy and potential toxicities. As the field of HCV therapy is rapidly evolving, readers should also refer to the latest drug product labels and 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.

Selected HIV Drugs	HCV Direct-Acting Antiviral Agents									
	NS5A Inhibitor	NS5B Inhibitor	Coformulated							
			<b>SHOULD NOT BE USED IN THOSE WITH MODERATE TO SEVERE HEPATIC IMPAIRMENT</b> (Cirrhosis classified as Child-Pugh class B or C)							
			NS5A/NS5B Inhibitor	NS5A/NS5B Inhibitor	NS5A/NS5B Inhibitor/ NS3/4A Protease Inhibitor	NS5A Inhibitor/ NS3/4A Protease Inhibitor	NS5A Inhibitor/ NS3A/4A Protease Inhibitor	NS5A Inhibitor/ NS3A/4A Protease Inhibitor plus NS5B Inhibitor	NS3A/4A Protease Inhibitor <sup>a</sup>	
Daclatasvir	Sofosbuvir	Ledipasvir/ Sofosbuvir	Sofosbuvir/ Velpatasvir	Sofosbuvir/ Velpatasvir/ Voxilaprevir	Glecaprevir/ Pibrentasvir	Elbasvir/ Grazoprevir	Ombitasvir/ Paritaprevir/ Ritonavir plus Dasabuvir <sup>a</sup>	Simeprevir		
<b>NRTIs</b>										
3TC	✓	✓	✓	✓	✓	✓	✓	✓	✓	
ABC	✓	✓	✓	✓	✓	✓	✓	✓	✓	
FTC	✓	✓	✓	✓	✓	✓	✓	✓	✓	
TDF	✓	✓	✓ Monitor for TDF toxicity.	✓ Monitor for TDF toxicity.	✓ Monitor for TDF toxicity.	✓	✓	✓	✓	
TAF	✓	✓	✓	✓	✓	✓	✓	✓	✓	
<b>PIs</b>										
Unboosted ATV	✓	✓	✓	✓	✗	✗	✗	✓ <sup>b</sup>	✗	



**Table 13. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of HCV in Adults with HIV** (page 2 of 4)

Selected HIV Drugs	HCV Direct-Acting Antiviral Agents									
	NS5A Inhibitor	NS5B Inhibitor	Coformulated							
			<b>SHOULD NOT BE USED IN THOSE WITH MODERATE TO SEVERE HEPATIC IMPAIRMENT</b> (Cirrhosis classified as Child-Pugh class B or C)							
			NS5A/NS5B Inhibitor	NS5A/NS5B Inhibitor	NS5A/NS5B Inhibitor/ NS3/4A Protease Inhibitor	NS5A Inhibitor/ NS3/4A Protease Inhibitor	NS5A Inhibitor/ NS3A/4A Protease Inhibitor	NS5A Inhibitor/ NS3A/4A Protease Inhibitor plus NS5B Inhibitor	NS3A/4A Protease Inhibitor <sup>a</sup>	
Daclatasvir	Sofosbuvir	Ledipasvir/ Sofosbuvir	Sofosbuvir/ Velpatasvir	Sofosbuvir/ Velpatasvir/ Voxilaprevir	Glecaprevir/ Pibrentasvir	Elbasvir/ Grazoprevir	Ombitasvir/ Paritaprevir/ Ritonavir plus Dasabuvir <sup>a</sup>	Simeprevir		
PIs, continued										
ATV/r or ATV/c	✓ ↓ DCV dose to 30 mg/day	✓			✗	✗	✗	✓ <sup>c</sup>	✗	
DRV/r or DRV/c	✓	✓	✓ If a PI/r or PI/c is used with TDF, ↑ TDF concentrations are expected. If coadministration is necessary, monitor for TDF-associated toxicities. <sup>d</sup>	✓ If a PI/r or PI/c is used with TDF, ↑ TDF concentrations are expected. If coadministration is necessary, monitor for TDF-associated toxicities. <sup>d</sup>	✓ If a PI/r is used with TDF, ↑ TDF concentrations. Monitor for TDF-associated toxicities. <sup>d</sup> Consider monitoring for hepatotoxicity. <sup>e</sup>	✗	✗	✗	✗	
LPV/r	✓	✓			✗	✗	✗	✗	✗	
TPV/r	?	✗	✗	✗	✗	✗	✗	✗	✗	
NNRTIs										
DOR	✓	✓	✓	✓	✓	✓	✓	✓	✓	
EFV	✓ ↑ DCV dose to 90 mg/day	✓	✓ If used with TDF, monitor for TDF toxicity.	✗	✗	✗	✗	✗	✗	
ETR	✓ ↑ DCV dose to 90 mg/day	✓		✗	✗	✗	✗	✗	✗	

**Table 13. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of HCV in Adults with HIV** (page 3 of 4)

Selected HIV Drugs	HCV Direct-Acting Antiviral Agents								
	NS5A Inhibitor	NS5B Inhibitor	Coformulated						NS3A/4A Protease Inhibitor <sup>a</sup>
			<b>SHOULD NOT BE USED IN THOSE WITH MODERATE TO SEVERE HEPATIC IMPAIRMENT</b> (Cirrhosis classified as Child-Pugh class B or C)						
			NS5A/NS5B Inhibitor	NS5A/NS5B Inhibitor	NS5A/NS5B Inhibitor/ NS3/4A Protease Inhibitor	NS5A Inhibitor/ NS3/4A Protease Inhibitor	NS5A Inhibitor/ NS3A/4A Protease Inhibitor	NS5A Inhibitor/ NS3A/4A Protease Inhibitor plus NS5B Inhibitor	
Daclatasvir	Sofosbuvir	Ledipasvir/ Sofosbuvir	Sofosbuvir/ Velpatasvir	Sofosbuvir/ Velpatasvir/ Voxilaprevir	Glecaprevir/ Pibrentasvir	Elbasvir/ Grazoprevir	Ombitasvir/ Paritaprevir/ Ritonavir plus Dasabuvir <sup>a</sup>	Simeprevir	
NNRTIs, continued									
NVP	✓ ↑ DCV dose to 90 mg/day	✓	✓ If used with TDF, monitor for TDF toxicity.	✗	✗	✗	✗	✗	✗
RPV	✓	✓		✓	✓	✓	✓	✗	✓
INSTIs									
BIC/TAF/FTC	✓	✓	✓	✓	✓	✓	✓	✓	✓
DTG	✓	✓	✓ If used with TDF, monitor for TDF toxicity.	✓	✓	✓	✓	✓	✓
EVG/c/TDF/FTC	✓ ↓ DCV dose to 30 mg/day	✓	✗	✓ If used with TDF, monitor for TDF toxicity.	✓ If used with TDF, monitor for TDF toxicity. Consider monitoring for hepatotoxicity. <sup>e</sup>	✓ If used with TDF, monitor for TDF toxicity. Consider monitoring for hepatotoxicity. <sup>f</sup>	✗	✗	✗
EVG/c/TAF/FTC	✓ ↓ DCV dose to 30 mg/day	✓	✓	✓	✓ Consider monitoring for hepatotoxicity. <sup>e</sup>	✓ Consider monitoring for hepatotoxicity. <sup>f</sup>	✗	✗	✗
RAL	✓	✓	✓	✓	✓	✓	✓	✓	✓
CCR5 Antagonist									
MVC	✓	✓	✓	✓	✓	✓	✓	✗	✓

**Table 13. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of HCV in Adults with HIV** (page 4 of 4)

<sup>a</sup> Dasabuvir must be prescribed with ombitasvir/paritaprevir/RTV.

<sup>b</sup> Reduce ATV dose to 300 mg and instruct the patient to take it in the morning at same time as ombitasvir/paritaprevir/RTV plus dasabuvir. If RTV cannot be used, choose an alternative HCV regimen.

<sup>c</sup> This HCV regimen contains RTV. If ATV is part of the ARV regimen, prescribe ATV 300 mg without COBI or RTV. It should be taken in the morning at the same time as ombitasvir/paritaprevir/RTV plus dasabuvir. Resume RTV or COBI regimen when HCV therapy is completed.

<sup>d</sup> Consider using an alternative HCV treatment or ARV regimen to avoid increases in TDF exposure. If co-administration is necessary, monitor patient for TDF-associated adverse reactions.

<sup>e</sup> Voxilaprevir exposures can increase when it is coadministered with pharmacologically boosted DRV or EVG. Until more safety data in clinical settings becomes available, patients who are receiving voxilaprevir and pharmacologically boosted DRV or EVG should be monitored for hepatotoxicity.

<sup>f</sup> Glecaprevir exposures can increase when it is coadministered with EVG/c. Until more safety data in clinical settings becomes available, patients who are receiving glecaprevir and EVG/c should be monitored for hepatotoxicity.

**Key to Symbols:**

✓ = ARV agents that can be used concomitantly

✗ = ARV agents not recommended

? = data limited or not available on pharmacokinetic interactions with ARV drug

↑ = increase

↓ = decrease

**Key to Acronyms:** 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; **BIC = bicitgravir**; COBI = cobicistat; DAA = direct-acting antiviral agents; DCV = daclatasvir; **DOR = doravirine**; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; DSV = dasabuvir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; FDA = Food and Drug Administration; EVG/c = elvitegravir/cobicistat; FPV = fosamprenavir; FTC = emtricitabine; HCV = hepatitis C virus; IDV = indinavir; INSTI = integrase strand transfer inhibitor; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PI/c = 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 14. Strategies to Improve Linkage to Care, Retention in Care, Adherence to Appointments, and Adherence to Antiretroviral Therapy** (page 1 of 2)

Strategies	Examples
Provide an accessible, trustworthy, nonjudgmental multidisciplinary health care team.	<ul style="list-style-type: none"> <li>• Care providers, nurses, social workers, case managers, pharmacists, and medication managers.</li> </ul>
Strengthen early linkage to care and retention in care.	<ul style="list-style-type: none"> <li>• Encourage health care team participation in linkage to and retention in care.</li> <li>• Use ARTAS training (if available).</li> </ul>
Evaluate patient's knowledge about HIV infection, prevention, and treatment and, based on this assessment, provide HIV-related information.	<ul style="list-style-type: none"> <li>• 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.</li> </ul>
Identify facilitators, potential barriers to adherence, and necessary medication management skills both before starting ART and on an ongoing basis.	<ul style="list-style-type: none"> <li>• Assess patient's cognitive competence and impairment.</li> <li>• 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.</li> <li>• Identify and address language and literacy barriers.</li> <li>• Assess beliefs, perceptions, and expectations about taking ART (e.g., impact on health, side effects, disclosure issues, consequences of poor adherence).</li> <li>• 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).</li> <li>• 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.</li> </ul>
Provide needed resources.	<ul style="list-style-type: none"> <li>• Provide or refer for mental health and/or substance abuse treatment.</li> <li>• Provide resources to obtain prescription drug coverage (e.g., Common Patient Assistance Program Application (CPAPA): <a href="http://bit.ly/CommonPAPForm">http://bit.ly/CommonPAPForm</a>; Pharmaceutical Company HIV Patient Assistance Programs and Cost-Sharing Assistance Programs: <a href="http://bit.ly/1XlahvN">http://bit.ly/1XlahvN</a>)</li> <li>• Provide resources about stable housing, social support, transportation assistance, and income and food security.</li> </ul>
Involve the patient in ARV regimen selection.	<ul style="list-style-type: none"> <li>• Review potential side effects, dosing frequency, pill burden, storage requirements, food requirements, and consequences of poor adherence.</li> <li>• Assess daily activities and tailor regimen to predictable and routine daily events.</li> <li>• Consider preferential use of PI/r-based or DTG-based ART if poor adherence is anticipated.</li> <li>• Consider use of STR formulations.</li> <li>• Assess if cost/copayment for drugs will affect adherence and access to medications.</li> </ul>
Assess adherence at every clinic visit.	<ul style="list-style-type: none"> <li>• Monitor viral load as a strong biologic measure of adherence.</li> <li>• Use a simple behavioral rating scale or self-reported assessment.</li> <li>• Employ a structured format that normalizes or assumes less-than-perfect adherence and minimizes socially desirable or "white-coat adherence" responses.</li> <li>• Ensure that other members of the health care team also assess and support adherence.</li> </ul>
Use positive reinforcement to foster adherence success.	<ul style="list-style-type: none"> <li>• Inform patients of low or nondetectable levels of HIV viral load and increases in CD4 cell counts.</li> <li>• Thank patients for attending their appointments.</li> </ul>

**Table 14. Strategies to Improve Linkage to Care, Retention in Care, Adherence to Appointments, and Adherence to Antiretroviral Therapy (page 2 of 2)**

Strategies	Examples
Identify the type of and reasons for poor adherence and target ways to improve adherence.	<ul style="list-style-type: none"> <li>• Failure to understand dosing instructions.</li> <li>• Complexity of regimen (e.g., pill burden, size, dosing schedule, food requirements, polypharmacy).</li> <li>• Pill aversion or pill fatigue.</li> <li>• Adverse effects.</li> <li>• Inadequate understanding of drug resistance and its relationship to adherence.</li> <li>• Patient is unaware of appointments or appointments are not scheduled with proper patient input.</li> <li>• Cost-related issues (copays for medications or visits, missed work time).</li> <li>• Depression, drug and alcohol use, homelessness, poverty.</li> <li>• Stigma of taking pills or attending HIV-related appointments.</li> <li>• Nondisclosure of status leading to missed doses, refills, or appointments.</li> </ul>
Select from among available effective adherence and retention interventions.	<ul style="list-style-type: none"> <li>• 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.</li> <li>• Use adherence-related tools to complement education and counseling interventions (e.g., text messaging, pill box monitors, pill boxes, alarms).</li> <li>• Use community resources to support adherence (e.g., visiting nurses, community workers, family, peer advocates, transportation assistance).</li> <li>• Use patient prescription assistance programs (see above, under “Provide needed resources”).</li> <li>• Use motivational interviews.</li> <li>• Provide outreach for patients who drop out of care</li> <li>• Use peer or paraprofessional treatment navigators.</li> <li>• Recognize positive clinical outcomes resulting from better adherence.</li> <li>• Arrange for DOT in persons in substance use treatment (if feasible).</li> <li>• Enhance clinic support and structures to promote linkage and retention (reminder calls, flexible scheduling, open access, active referrals, and improved patient satisfaction).</li> </ul>
Systematically monitor retention in care.	<ul style="list-style-type: none"> <li>• Record and follow up on missed visits.</li> </ul>

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

“N/A” indicates either that there are no reported cases for that particular side effect or that data for that specific ARV drug class are not available. See [Appendix B](#) for additional information listed by drug.

Adverse Effect	Drug Class				
	NRTIs	NNRTIs	PIs	INSTIs	EIs
<b>Bleeding Events</b>	N/A	N/A	Spontaneous bleeding, hematuria in hemophilia  <u>TPV</u> : Intracranial hemorrhage is associated with CNS lesions, trauma, alcohol abuse, hypertension, coagulopathy, anticoagulant or antiplatelet agents, and the use of vitamin E supplements.	N/A	N/A
<b>Bone Density Effects</b>	<u>TDF</u> : Associated with greater loss of BMD than other NRTIs. Osteomalacia may be associated with renal tubulopathy and urine phosphate wasting.  <u>TAF</u> : Associated with smaller declines in BMD than those seen with TDF.	Decreases in BMD observed after the initiation of any ART regimen.			N/A
<b>Bone Marrow Suppression</b>	<u>ZDV</u> : Anemia, neutropenia	N/A	N/A	N/A	N/A
<b>Cardiac Conduction Effects</b>	N/A	<u>RPV, EFV</u> : QTc prolongation	<u>SQV/r, ATV/r, and LPV/r</u> : PR prolongation. Risk factors include pre-existing heart disease and the use of other medications.  <u>SQV/r</u> : QT prolongation. Obtain ECG before administering SQV.	N/A	N/A
<b>Cardiovascular Disease</b>	<u>ABC and ddI</u> : Associated with an increased risk of MI in some cohort studies. Absolute risk greatest in patients with traditional CVD risk factors.	N/A	<u>DRV, FPV, IDV, and LPV/r</u> : Associated with cardiovascular events in some cohorts	N/A	N/A
<b>Cholelithiasis</b>	N/A	N/A	<u>ATV</u> : Cholelithiasis and kidney stones may present concurrently. Median onset is 42 months.	N/A	N/A

**Table 15. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy (page 2 of 5)**

Adverse Effect	Drug Class				
	NRTIs	NNRTIs	PIs	INSTIs	EIs
<b>Diabetes Mellitus and Insulin Resistance</b>	ZDV, d4T, and ddI	N/A	Reported for some (IDV, LPV/r), but not all, PIs.	N/A	N/A
<b>Dyslipidemia</b>	d4T > ZDV > ABC: ↑ TG and LDL  TAF: ↑ TG, ↑ LDL, ↑ HDL (no change in TC:HDL ratio)  TDF has been associated with lower lipid levels than ABC or TAF.	EFV: ↑ TG, ↑ LDL, ↑ HDL	All RTV- or COBI-Boosted PIs: ↑ TG, ↑ LDL, ↑ HDL  LPV/r and FPV/r > DRV/r and ATV/r: ↑ TG	EVG/c: ↑ TG, ↑ LDL, ↑ HDL	N/A
<b>Gastrointestinal Effects</b>	ddI and ZDV > Other NRTIs: Nausea and vomiting  ddI: Pancreatitis	N/A	GI intolerance (e.g., diarrhea, nausea, vomiting)  NFV and LPV/r > DRV/r and ATV/r: Diarrhea	EVG/c: Nausea and diarrhea	IBA: 8% of patients reported diarrhea in a study of 40 people.
<b>Hepatic Effects</b>	<b>Reported with most NRTIs.</b>  <u>ZDV, d4T, and ddI</u> : Steatosis  ddI: Prolonged exposure linked to noncirrhotic portal hypertension and esophageal varices.  <u>When TAF, TDF, 3TC, and FTC are Withdrawn in Patients with HBV/HIV Coinfection or When HBV Resistance Develops</u> : Patients with HBV/HIV coinfection may develop severe hepatic flares.	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 >250 cells/mm <sup>3</sup> and men with pre-NVP CD4 counts >400 cells/mm <sup>3</sup> .  NVP should <b>never</b> be used for post-exposure prophylaxis.  EFV and NVP <b>are not recommended</b> in patients with hepatic insufficiency (Child-Pugh class B or C).	All PIs: Drug-induced hepatitis and hepatic decompensation have been reported; greatest frequency occurs with TPV/r.  TPV/r: <b>Contraindicated</b> in patients with hepatic insufficiency (Child Pugh class B or C).  IDV and ATV: Jaundice due to indirect hyperbilirubinemia	N/A	MVC: Hepatotoxicity with or without rash or HSRs reported.

**Table 15. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy** (page 3 of 5)

Adverse Effect	Drug Class				
	NRTIs	NNRTIs	PIs	INSTIs	EIs
<p><b>Hypersensitivity Reaction</b></p> <p>Excluding rash alone or Stevens-Johnson syndrome</p>	<p><b>ABC: Contraindicated</b> if patient is HLA-B*5701 positive.</p> <p>Median onset for HSR is 9 days; 90% of reactions occur within first 6 weeks of treatment.</p> <p><u>HSR Symptoms (in Order of Descending Frequency):</u> Fever, rash, malaise, nausea, headache, myalgia, chills, diarrhea, vomiting, abdominal pain, dyspnea, arthralgia, and respiratory symptoms</p> <p>Symptoms worsen with continuation of ABC.</p> <p>Patients should not be rechallenged with ABC if HSR is suspected, regardless of their HLA-B*5701 status.</p>	<p><b>NVP:</b> 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.</p> <p>Risk is greater for ARV-naive women with pre-NVP CD4 counts &gt;250 cells/mm<sup>3</sup> and men with pre-NVP CD4 counts &gt;400 cells/mm<sup>3</sup>. Overall, risk is higher for women than men.</p> <p>A 2-week dose escalation of NVP reduces risk.</p>	N/A	<p><b>RAL:</b> HSR reported when RAL is given with other drugs also known to cause HSRs. All ARVs should be stopped if HSR occurs.</p> <p><b>DTG:</b> Reported in &lt;1% of patients in clinical development program</p>	<p><b>MVC:</b> HSR reported as part of a syndrome related to hepatotoxicity.</p>
<p><b>Lactic Acidosis</b></p>	<p><u>Reported with NRTIs, Especially d4T, ZDV, and ddI:</u> Insidious onset with GI prodrome, weight loss, and fatigue. May rapidly progress with tachycardia, tachypnea, jaundice, weakness, mental status changes, pancreatitis, and organ failure. Mortality high if serum lactate &gt;10 mmol/L.</p> <p>Women and obese patients at increased risk.</p>	N/A	N/A	N/A	N/A
<p><b>Lipodystrophy</b></p>	<p><u>Lipoatrophy:</u> d4T &gt; ZDV. More likely when NRTIs are coadministered with EFV than with an RTV-boosted PI.</p>	<p><u>Lipohypertrophy:</u> Trunk fat increase observed with EFV-, PI-, and RAL-containing regimens; however, causal relationship has not been established.</p>			N/A



**Table 15. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy** (page 4 of 5)

Adverse Effect	Drug Class				
	NRTIs	NNRTIs	PIs	INSTIs	EIs
<b>Myopathy/ Elevated Creatine Phosphokinase</b>	<u>ZDV</u> : Myopathy	N/A	N/A	<u>RAL</u> and <u>DTG</u> : ↑ CPK, rhabdomyolysis, and myopathy or myositis have been reported.	N/A
<b>Nervous System/ Psychiatric Effects</b>	<u>d4T</u> > <u>ddI</u> : Peripheral neuropathy (can be irreversible)  <u>d4T</u> : Associated with rapidly progressive, ascending neuromuscular weakness resembling Guillain-Barré syndrome (rare)	<b>Neuropsychiatric Events: EFV &gt; RPV, DOR &gt; ETR</b>  <u>EFV</u> : Somnolence, insomnia, abnormal dreams, dizziness, impaired concentration, depression, psychosis, and suicidal ideation. Symptoms usually subside or diminish after 2–4 weeks. Bedtime dosing may reduce symptoms. Risk factors include presence of psychiatric illness, concomitant use of agents with neuropsychiatric effects, and increased EFV concentrations because of genetic factors or increased absorption with food. An association between EFV and suicidal ideation, suicide, and attempted suicide was found in a retrospective analysis of comparative trials.  <u>RPV</u> : Depression, suicidality, sleep disturbances  <u>DOR</u> : Sleep disorders and disturbances, dizziness, altered sensorium; depression and suicidality/self-harm	N/A	<b>All INSTIs</b> : Insomnia, depression, and suicidality have been reported with INSTI use, primarily in patients with pre-existing psychiatric conditions.	N/A
<b>Rash</b>	<u>FTC</u> : Hyperpigmentation	All NNRTIs	ATV, DRV, FPV, LPV/r, and TPV	All INSTIs	MVC, <b>IBA</b>

**Table 15. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy** (page 5 of 5)

Adverse Effect	Drug Class				
	NRTIs	NNRTIs	PIs	INSTIs	EIs
<b>Renal Effects/ Urolithiasis</b>	<p><u>TDF</u>: ↑ 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.</p> <p><u>TAF</u>: Less impact on renal biomarkers and lower rates of proteinuria than TDF.</p>	<p><u>RPV</u>: Inhibits Cr secretion without reducing renal glomerular function.</p>	<p><u>ATV and LPV/r</u>: Associated with increased risk of chronic kidney disease in a large cohort study.</p> <p><u>IDV</u>: ↑ SCr, pyuria, renal atrophy, or hydronephrosis</p> <p><u>IDV, ATV</u>: Stone or crystal formation. Adequate hydration may reduce risk.</p> <p><u>COBI (as a Boosting Agent for DRV or ATV)</u>: Inhibits Cr secretion without reducing renal glomerular function.</p>	<p><u>DTG, COBI (as a Boosting Agent for EVG), and BIC</u>: Inhibits Cr secretion without reducing renal glomerular function</p>	<p><u>IBA</u>: SCr abnormalities ≥Grade 3 reported in 10% of trial participants.</p>
<b>Stevens-Johnson Syndrome/ Toxic Epidermal Necrosis</b>	<p>Some reported cases for ddl and ZDV.</p>	<p>NVP &gt; DLV, EFV, ETR, RPV</p>	<p>Some reported cases for FPV, DRV, IDV, LPV/r, and ATV.</p>	<p>RAL</p>	<p>N/A</p>

**Key to Acronyms:** 3TC = lamivudine; ABC = abacavir; ART= antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/r = atazanavir/ritonavir; **BIC = bicitgravir**; BMD = bone mineral density; CD4 = CD4 T lymphocyte; Cr = creatinine; CNS = central nervous system; COBI = cobicistat; CPK = creatine phosphokinase; CVD = cardiovascular disease; d4T = stavudine; ddl = didanosine; DLV = delavirdine; **DOR = doravirine**; DRV = darunavir; DRV/r = darunavir/ritonavir; DTG = dolutegravir; ECG = electrocardiogram; EFV = efavirenz; EI = entry inhibitor; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FPV = fosamprenavir; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; GI = gastrointestinal; HBV = hepatitis B virus; HDL = high-density lipoprotein; HSR = hypersensitivity reaction; **IBA = ibalizumab**; IDV = indinavir; INSTI = integrase strand transfer inhibitor; LDL = low-density lipoprotein; LPV/r = lopinavir/ritonavir; MI = myocardial infarction; MVC = maraviroc; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SCr = serum creatinine; SQV = saquinavir; SQV/r = saquinavir/ritonavir; TAF = tenofovir alafenamide; TC = total cholesterol; TDF = tenofovir disoproxil fumarate; TG = triglycerides; TPV = tipranavir; TPV/r = tipranavir/ritonavir; ZDV = zidovudine

**Table 16. Antiretroviral Therapy-Associated Adverse Events That Can Be Managed with Substitution of Alternative Antiretroviral Agent** (page 1 of 3)

Adverse Event	ARV Agent(s) or Drug Class		Comments
	Switch from	Switch to	
<b>Bone Density Effects</b>	TDF <sup>a</sup>	TAF or ABC <sup>b</sup>  NRTI-sparing regimens or regimens using only 3TC or FTC as the NRTI may be considered, if appropriate.	Declines in BMD have been observed upon initiation of most ART regimens. Switching from TDF to alternative ARV agents has been shown to increase bone density, but the clinical significance of this increase remains uncertain.  TAF is associated with smaller declines in BMD than TDF, and patients show improvement in BMD upon switching to TAF. The long-term impact of TAF on patients with osteopenia or osteoporosis is unknown; close clinical monitoring is recommended in this setting.
<b>Bone Marrow Suppression</b>	ZDV	TDF, TAF, or ABC <sup>b</sup>	ZDV has been associated with neutropenia and macrocytic anemia.
<b>Cardiac QTc Interval Prolongation</b>	EFV, RPV	A PI- or INSTI-based regimen	High EFV and RPV exposures may cause QT prolongation.  Consider switching from EFV- or RPV-based regimens if patient is taking other medications with known risk of Torsades de Pointes, or in patients at higher risk of Torsades de Pointes.
<b>Cardiovascular Events</b>  Myocardial infarction, ischemic stroke	ABC	TDF, TAF, FTC, or 3TC	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.
	RTV- or COBI-boosted PI regimens, EFV, EVG/c	RAL, DTG, <b>BIC</b> , or RPV	RAL, DTG, <b>BIC</b> , and RPV have less effect on lipids than RTV- or COBI-boosted PI regimens, EFV, and EVG/c.  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.
<b>Central Nervous System, Neuropsychiatric Side Effects</b>  Dizziness, suicidal ideation, abnormal dreams, depression	EFV, RPV	ETR, PI/c, or PI/r  INSTIs may be used, but monitoring is recommended (see Comments column).	In most patients, EFV-related CNS effects subside within 4 weeks after initiation of the drug. Persistent or intolerable effects should prompt substitution of EFV.  INSTIs are associated with insomnia. Depression and suicidality have been infrequently reported with INSTI use, primarily in patients with pre-existing psychiatric conditions.
<b>Dyslipidemia</b>  Hypertriglyceridemia (with or without elevated LDL level)	RTV- or COBI-boosted regimens, and EFV	RAL, DTG, <b>BIC</b> , or RPV	Elevated TG and LDL levels are more common with LPV/r and FPV/r than with other RTV-boosted PIs. Improvements in TG and LDL levels have been observed with switch from LPV/r to ATV or ATV/r. <sup>c</sup>

**Table 16. Antiretroviral Therapy-Associated Adverse Events That Can Be Managed with Substitution of Alternative Antiretroviral Agent** (page 2 of 3)

Adverse Event	ARV Agent(s) or Drug Class		Comments
	Switch from	Switch to	
<b>Gastrointestinal Effects</b> Nausea, diarrhea	LPV/r	ATV/c, ATV/r, DRV/c, DRV/r, RAL, DTG, <b>BIC</b> , or EVG/c	GI intolerance is common with boosted PIs and is linked to the total dose of RTV. More GI toxicity is seen with LPV/r than with ATV/r or DRV/r. GI effects are often transient and do not warrant substitution unless they are persistent and intolerable.
	Other RTV- or COBI-boosted regimens	RAL, DTG, <b>BIC</b> , or NNRTIs	In a trial of treatment-naïve patients, rates of diarrhea and nausea were similar for EVG/c/TDF/FTC and ATV/r plus TDF/FTC.
<b>Hypersensitivity Reaction</b>	ABC	TDF or TAF	Never rechallenge with ABC following a suspected HSR, regardless of the patient's HLA-B*5701 status.
	NVP, EFV, ETR, RPV	Non-NNRTI ART	Risk of HSR with NVP is higher for women and those with high CD4 cell counts.
	DTG, RAL	Non-INSTI ART	Reactions to NVP, ETR, RAL, DTG, and MVC may be accompanied by elevated liver transaminases.
	MVC	Suitable alternative ART	
<b>Insulin Resistance</b>	LPV/r, FPV/r	INSTI, NNRTI	Results of switch studies have been inconsistent. Studies in HIV-negative patients suggest a direct causal effect of LPV/r (and IDV) on insulin resistance. However, traditional risk factors may be stronger risk factors for insulin resistance than the use of any PI.
<b>Jaundice and Icterus</b>	ATV, ATV/c, ATV/r	DRV/c, DRV/r, INSTI, or NNRTI	Increases in unconjugated bilirubin are common with ATV and generally do not require modification of therapy unless resultant symptoms are distressing to the patient.
<b>Lipoatrophy</b> Subcutaneous fat wasting of limbs, face, buttocks	d4T, ZDV	TDF, TAF, or ABC <sup>b</sup>	Peripheral lipoatrophy is associated with prior thymidine analog (d4T and ZDV) use. Switching from these ARVs prevents worsening lipoatrophy, but fat recovery is typically slow (may take years) and incomplete.
<b>Lipohypertrophy</b>	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 weight or visceral fat gain.		
<b>Rash</b>	NNRTIs (especially NVP and EFV)	PI- or INSTI-based regimen	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.
	DRV/c, DRV/r	ATV/c, ATV/r, or another drug class (e.g., INSTI)	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.

**Table 16. Antiretroviral Therapy-Associated Adverse Events That Can Be Managed with Substitution of Alternative Antiretroviral Agent** (page 3 of 3)

Adverse Event	ARV Agent(s) or Drug Class		Comments
	Switch from	Switch to	
<b>Renal Effects</b> Including proximal renal tubulopathy and elevated creatinine	TDF <sup>a</sup>	ABC, <sup>b</sup> TAF (for patients with CrCl >30 mL/min), NRTI-sparing regimens, or regimens using only 3TC or FTC as the NRTI may be considered if appropriate.	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.
	ATV/c, ATV/r, LPV/r	DTG, <b>BIC</b> , RAL, or NNRTI	COBI, DTG, <b>BIC</b> , 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 >0.4 mg/dL.
<b>Stones</b> Nephrolithiasis and cholelithiasis	ATV, ATV/c, ATV/r	DRV/c, DRV/r, INSTI, or NNRTI	This switch should be made if the clinician believes ATV is the cause of the stones.

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

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

<sup>c</sup> TDF reduces ATV levels; therefore, unboosted ATV should not be coadministered with TDF.

**Key to Acronyms:** 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 17. Monthly Average Prices of Commonly Used Antiretroviral Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 1 of 5)**

Prescription drug pricing in the United States involves complex systems of negotiations, rebates, discounts, and reimbursement rates. Much of the information used to determine drug prices is confidential, and prices can vary depending on the purchaser, the type of public or private insurance coverage in use, and the number of generic competitors. In addition, price increases that exceed rates of inflation can trigger additional rebates for Medicaid and 340B Drug Discount Program entities. Table 17 includes three benchmark prices, rounded to the nearest dollar, for commonly used antiretroviral (ARV) drugs<sup>a</sup> as a general reference for health care providers when considering the cost of HIV treatment. Health care providers should contact patients' pharmacies or payors regarding actual prices, comparative cost savings, and related formulary restrictions.

**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 ARVs, 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, 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 AWP are generally set annually, FULs are adjusted monthly, 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.

ARV Drug (Generic and Brand Names)	Strength, Formulation	Tablets, Capsules, or mLs per Month	WAC (Monthly) <sup>b</sup>	AWP (Monthly) <sup>b</sup>	FUL (As of 9/1/2018) <sup>c</sup>
<b>Nucleoside Reverse Transcriptase Inhibitors (NRTIs)</b>					
<b>Abacavir</b>					
• Generic	300 mg tablet	60 tablets	\$150 to \$482	\$579 to \$603	\$44
• Ziagen	300 mg tablet	60 tablets	\$559	\$670	
<b>Emtricitabine</b>					
• Emtriva	200 mg capsules	30 capsules	\$537	\$644	N/A
<b>Lamivudine</b>					
• Generic	300 mg tablet	30 tablets	\$75 to \$343	\$429 to \$430	\$83
• Epivir	300 mg tablet	30 tablets	\$416	\$499	

**Table 17. Monthly Average Prices of Commonly Used Antiretroviral Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)**  
(page 2 of 5)

ARV Drug (Generic and Brand Names)	Strength, Formulation	Tablets, Capsules, or mLs per Month	WAC (Monthly) <sup>b</sup>	AWP (Monthly) <sup>b</sup>	FUL (As of 9/1/2018) <sup>c</sup>
<b>Nucleoside Reverse Transcriptase Inhibitors (NRTIs), continued</b>					
<b>Tenofovir Disoproxil Fumarate</b>					
• <b>Generic</b>	<b>300 mg tablet</b>	<b>30 tablets</b>	<b>\$58 to \$922</b>	<b>\$110 to \$1,216</b>	<b>Pending</b>
• Viread	300 mg tablet	30 tablets	\$1,140	\$1,368	
<b>Zidovudine</b>					
• Generic	300 mg tablet	60 tablets	\$36 to \$54	\$54 to \$365	\$13
<b>NRTI Combination Products</b>					
<b>Abacavir/Lamivudine</b>					
• Generic	600 mg/300 mg tablets	30 tablets	\$185 to \$1,116	\$1,395	\$356
• Epzicom	600 mg/300 mg tablets	30 tablets	\$1,292	\$1,550	
<b>Tenofovir Alafenamide/Emtricitabine</b>					
• Descovy	25 mg/200 mg tablet	30 tablets	\$1,676	\$2,011	N/A
<b>Tenofovir Disoproxil Fumarate/Emtricitabine</b>					
• Truvada	300 mg/200 mg tablet	30 tablets	\$1,676	\$2,011	N/A
<b>Tenofovir Disoproxil Fumarate/Lamivudine</b>					
• <b>Cimduo</b>	<b>300 mg/300 mg tablet</b>	<b>30 tablets</b>	<b>\$1,005</b>	<b>\$1,207</b>	<b>N/A</b>
<b>Zidovudine/Lamivudine</b>					
• Generic	300 mg/150 mg tablet	60 tablets	\$134 to \$578	\$878 to \$932	\$47
• Combivir	300 mg/150 mg tablet	60 tablets	\$901	\$1,082	
<b>Abacavir Sulfate/Zidovudine/Lamivudine</b>					
• Generic	300 mg/300 mg/150 mg tablet	60 tablets	\$1,391	\$1,738	Pending
• Trizivir	300 mg/300 mg/150 mg tablet	60 tablets	\$1,610	\$1,932	
<b>Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)</b>					
<b>Efavirenz</b>					
• <b>Generic</b>	<b>600 mg tablet</b>	<b>30 tablets</b>	<b>\$894</b>	<b>\$1,118</b>	<b>Pending</b>
• Sustiva	600 mg tablet	30 tablets	\$981	\$1,177	
<b>Doravirine</b>					
• <b>Pifeltro</b>	<b>100 mg tablet</b>	<b>30 tablets</b>	<b>\$1,380</b>	<b>\$1,656</b>	<b>N/A</b>

**Table 17. Monthly Average Prices of Commonly Used Antiretroviral Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)**  
(page 3 of 5)

ARV Drug (Generic and Brand Names)	Strength, Formulation	Tablets, Capsules, or mLs per Month	WAC (Monthly) <sup>b</sup>	AWP (Monthly) <sup>b</sup>	FUL (As of 9/1/2018) <sup>c</sup>
<b>Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs), continued</b>					
<b>Etravirine</b> • Intence	200 mg tablet	60 tablets	\$1,296	\$1,523	N/A
<b>Nevirapine</b> • Generic	200 mg tablet	60 tablets	\$10 to \$45	\$648 to \$651	\$37
• Viramune	200 mg tablet	60 tablets	\$855	\$1,026	
• <b>Generic XR</b>	<b>400 mg tablet</b>	<b>30 tablets</b>	<b>\$246 to \$565</b>	<b>\$678 to \$706</b>	\$231
• Viramune XR	400 mg tablet	30 tablets	\$793	\$951	
<b>Rilpivirine</b> • Edurant	25 mg tablet	30 tablets	\$1043	\$1,252	N/A
<b>Protease Inhibitors (PIs)</b>					
<b>Atazanavir</b> • <b>Generic</b>	<b>200 mg capsule</b>	<b>60 capsules</b>	<b>\$878 to \$1,264</b>	<b>\$1,580 to \$1,668</b>	<b>Pending</b>
• Reyataz	200 mg capsule	60 capsules	\$1,463	\$1,756	
• <b>Generic</b>	<b>300 mg capsule</b>	<b>30 capsules</b>	<b>\$870 to \$1,252</b>	<b>\$1,565 to \$1,652</b>	<b>Pending</b>
• Reyataz	300 mg capsule	30 capsules	\$1,449	\$1,739	
<b>Atazanavir/Cobicistat</b> • Evotaz	300/150 mg tablet	30 tablets	\$1,605	\$1,927	N/A
<b>Darunavir</b> • Prezista	600 mg tablet	60 tablets	\$1,581	\$1,897	N/A
• Prezista	800 mg tablet	30 tablets	\$1,581	\$1,897	N/A
• Prezista	100 mg/mL suspension	200 mL	\$878	\$1,054	N/A
<b>Darunavir/Cobicistat</b> • Prezcobix	800 mg/150 mg tablet	30 tablets	\$1,806	\$2,168	N/A
<b>Lopinavir/Ritonavir</b> • Kaletra	200 mg/50 mg tablet	120 tablets	\$1,024	\$1,229	N/A
<b>Tipranavir</b> • Aptivus	250 mg capsule	120 capsules	\$1,578	\$1,894	N/A



**Table 17. Monthly Average Prices of Commonly Used Antiretroviral Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)**  
(page 4 of 5)

ARV Drug (Generic and Brand Names)	Strength, Formulation	Tablets, Capsules, or mLs per Month	WAC (Monthly) <sup>b</sup>	AWP (Monthly) <sup>b</sup>	FUL (As of 9/1/2018) <sup>c</sup>
<b>Integrase Strand Transfer Inhibitors (INSTIs)</b>					
<b>Dolutegravir</b>					
• Tivicay	50 mg tablet	30 tablets	\$1,658	\$1,989	N/A
• Tivicay	50 mg tablet	60 tablets	\$3,315	\$3,978	N/A
<b>Raltegravir</b>					
• Isentress	400 mg tablet	60 tablets	\$1,500	\$1,800	N/A
• Isentress HD	600 mg tablet	60 tablets	\$1,500	\$1,800	N/A
<b>Fusion Inhibitor</b>					
<b>Enfuvirtide</b>					
• Fuzeon	90 mg injection kit	60 doses (1 kit)	\$3,586	\$4,303	N/A
<b>CCR5 Antagonist</b>					
<b>Maraviroc</b>					
• Selzentry	150 mg tablet	60 tablets	\$1,511	\$1,813	N/A
• Selzentry	300 mg tablet	60 tablets	\$1,511	\$1,813	N/A
• Selzentry	300 mg tablet	120 tablets	\$3,022	\$3,626	N/A
<b>CD4-Directed Post-Attachment Inhibitor</b>					
<b>Ibalizumab-uiyk</b>					
• Trogarzo	200 mg vials	8 vials	\$9,080	\$10,896	N/A
<b>Coformulated Combination Products as Single Tablet Regimens</b>					
<b>Bictegravir/Tenofovir Alafenamide/Emtricitabine</b>					
• Biktarvy	50 mg/25 mg/200 mg	30 tablets	\$2,946	\$3,535	N/A
<b>Dolutegravir/Abacavir/Lamivudine</b>					
• Triumeq	50 mg/600 mg/300 mg tablet	30 tablets	\$2,805	\$3,366	N/A
<b>Dolutegravir/Rilpivirine</b>					
• Juluca	50 mg/25 mg	30 tablets	\$2,579	\$3,095	N/A
<b>Doravirine/Tenofovir Disoproxil Fumarate/Lamivudine</b>					
• Delstrigo	100 mg/300 mg/300 mg	30 tablets	\$2,100	\$2,520	N/A
<b>Efavirenz/Tenofovir Disoproxil Fumarate/Emtricitabine</b>					
• Atripla	600 mg/300 mg/200 mg tablet	30 tablets	\$2,724	\$3,269	N/A

**Table 17. Monthly Average Prices of Commonly Used Antiretroviral Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)**  
(page 5 of 5)

ARV Drug (Generic and Brand Names)	Strength, Formulation	Tablets, Capsules, or mLs per Month	WAC (Monthly) <sup>b</sup>	AWP (Monthly) <sup>b</sup>	FUL (As of 9/1/2018) <sup>c</sup>
<b>Coformulated Combination Products as Single Tablet Regimens, continued</b>					
<b>Efavirenz/Tenofovir Disoproxil Fumarate/Lamivudine</b>					
• Symfi	600 mg/300 mg/150 mg tablet	30 tablets	\$1,634	\$1,961	N/A
• Symfi Lo	400 mg/300 mg/150 mg tablet	30 tablets	\$1,634	\$1,961	N/A
<b>Elvitegravir/Cobicistat/Tenofovir Alafenamide/Emtricitabine</b>					
• Genvoya	150 mg/150 mg/10 mg/200 mg tablet	30 tablets	\$2,946	\$3,535	N/A
<b>Elvitegravir/Cobicistat/Tenofovir Disoproxil Fumarate/Emtricitabine</b>					
• Stribild	150 mg/150 mg/300 mg/200 mg tablet	30 tablets	\$3,090	\$3,708	N/A
<b>Rilpivirine/Tenofovir Alafenamide/Emtricitabine</b>					
• Odefsey	25 mg/25 mg/200 mg tablet	30 tablets	\$2,681	\$3,217	N/A
<b>Rilpivirine/Tenofovir Disoproxil Fumarate/Emtricitabine</b>					
• Complera	25 mg/300 mg/200 mg tablet	30 tablets	\$2,681	\$3,217	N/A
<b>Pharmacokinetic Enhancers (Boosters)</b>					
<b>Cobicistat</b>					
• Tybost	150 mg tablet	30 tablets	\$219	\$264	N/A
<b>Ritonavir</b>					
• Generic	100 mg tablet	30 tablets	\$222	\$278	Pending
• Norvir	100 mg tablet	30 tablets	\$257	\$309	

<sup>a</sup> The following less commonly used ARV drugs are not included in this table: delavirdine, didanosine, fosamprenavir, indinavir, nelfinavir, saquinavir, and stavudine.

<sup>b</sup> Source: IBM Watson Health. Micromedex Red Book [database]. 2018. Available at: <https://www.micromedexsolutions.com>

<sup>c</sup> Source: Medicare & Medicaid Services. Federal Upper Limits—September 2018 [database]. 2018 September 1. Available at: <https://www.medicare.gov/medicaid/prescription-drugs/pharmacy-pricing/index.html>.

**Table 18. Mechanisms of Antiretroviral-Associated Drug Interactions (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 1 of 2)

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

**Note:** N/A indicates that there are no clinically relevant interactions by these mechanisms. **Identified mechanisms are specific to individual ARV drugs and not combinations of ARV drugs.**

ARV Drugs by Drug Class	Mechanisms That May Affect Oral Absorption of ARV Drugs			Enzymes That Metabolize or are Induced or Inhibited by ARV Drugs				Other Mechanisms of Known Drug Interactions
	Increasing Gastric pH	Cationic Chelation	P-glyco-protein	CYP Substrate	CYP Inhibitor	CYP Inducer	UGT1A1	
<b>INSTIs</b>								
<b>BIC</b>	N/A	Concentration decreased by products that contain polyvalent cations (e.g., Ca, Mg, Al, Fe, Zn)	Substrate	3A4	N/A	N/A	Substrate	Inhibitor of renal transporters OCT2 and MATE1
<b>DTG</b>	N/A		Substrate	3A4 (minor)	N/A	N/A	Substrate	Inhibitor of renal transporters OCT2 and MATE1
<b>EVG</b>	N/A		N/A	3A4	N/A	2C9	Substrate	N/A
<b>RAL</b>	N/A		N/A	N/A	N/A	N/A	Substrate	N/A
<b>PK Enhancers (Boosters)</b>								
<b>COBI</b>	N/A	N/A	Inhibitor	3A4	3A4, 2D6	N/A	N/A	N/A
<b>RTV</b>	N/A	N/A	Substrate, inhibitor	3A4, 2D6	3A4, 2D6	1A2, 2B6, 2C8, 2C9, 2C19	Inducer	N/A
<b>PIs</b>								
<b>Note:</b> When PIs are coadministered with PK enhancers (boosters), the pharmacologic properties of both agents should be considered when assessing potential drug interactions.								
<b>ATV</b>	Concentration decreased	N/A	Substrate, inducer, inhibitor	3A4	3A4	N/A	Inhibitor	OATP inhibitor
<b>DRV</b>	N/A	N/A	Substrate, inducer	3A4	3A4	2C9	N/A	OATP inhibitor
<b>FPV</b>	Concentration decreased by H2 antagonist	N/A	Substrate, inhibitor	3A4	3A4	N/A	N/A	N/A
<b>LPV</b>	N/A	N/A	Substrate	3A4	3A4	N/A	N/A	OATP inhibitor
<b>SQV</b>	N/A	N/A	Substrate, inhibitor	3A4	3A4	N/A	N/A	OATP inhibitor
<b>TPV</b>	N/A	N/A	Substrate, inducer	3A4	2D6	3A4, 1A2, 2C19	N/A	OATP inhibitor
<b>NNRTIs</b>								
<b>DOR</b>	N/A	N/A	N/A	3A4, 3A5	N/A	N/A	N/A	N/A
<b>EFV</b>	N/A	N/A	N/A	2B6 (primary), 2A6, 3A4	3A4	3A4, 2B6, 2C19	N/A	N/A

**Table 18. Mechanisms of Antiretroviral-Associated Drug Interactions (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 2 of 2)

ARV Drugs by Drug Class	Mechanisms That May Affect Oral Absorption of ARV Drugs			Enzymes That Metabolize or are Induced or Inhibited by ARV Drugs				Other Mechanisms of Known Drug Interactions
	Increasing Gastric pH	Cationic Chelation	P-glyco-protein	CYP Substrate	CYP Inhibitor	CYP Inducer	UGT1A1	
<b>NNRTIs, continued</b>								
<b>ETR</b>	N/A	N/A	N/A	3A4, 2C9, 2C19	2C9, 2C19	3A4	N/A	N/A
<b>NVP</b>	N/A	N/A	N/A	3A4, 2B6	N/A	3A4, 2B6	N/A	N/A
<b>RPV</b>	Concentration decreased	N/A	N/A	3A4	N/A	N/A	N/A	N/A
<b>NRTIs</b>								
<b>ABC</b>	N/A	N/A	N/A	N/A	N/A	N/A	Substrate	Alcohol dehydrogenase substrate
<b>FTC</b>	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
<b>3TC</b>	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
<b>TAF</b>	N/A	N/A	Substrate	N/A	N/A	N/A	N/A	OATP substrate
<b>TDF</b>	N/A	N/A	Substrate	N/A	N/A	N/A	N/A	Competition of active renal tubular secretion
<b>ZDV</b>	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Glucuronidation
<b>CCR5 Antagonist</b>								
<b>MVC</b>	N/A	N/A	Substrate	3A4	N/A	N/A	N/A	N/A
<b>Fusion Inhibitor</b>								
<b>T-20</b>	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

**Key to Acronyms:** 3TC = lamivudine; ABC = abacavir; Al = aluminum; ARV = antiretroviral; ATV = atazanavir; **BIC = bictegravir**; Ca = calcium; COBI = cobicistat; CYP = cytochrome P; **DOR = doravirine**; DRV = darunavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; Fe = iron; FPV = fosamprenavir; FTC = emtricitabine; INSTI = integrase strand transfer inhibitor; LPV = lopinavir; MATE = multidrug and toxin extrusion transporter; Mg = magnesium; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitors; NRTI = nucleoside reverse transcriptase inhibitors; NVP = nevirapine; OCT2 = organic cation transporter 2; OATP = organic anion-transporting polypeptide; PK = pharmacokinetic; PI = protease inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQV = saquinavir; T-20 = enfuvirtide; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV = tipranavir; UGT = uridine diphosphate glucuronosyltransferase; ZDV = zidovudine; Zn = zinc

**Table 19a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 1 of 19)

This table provides known or predicted information regarding PK interactions between PIs and non-ARV drugs. When information is available, interactions for PK-boosted (with either RTV or COBI) and unboosted ATV are listed separately. The term “All PIs” refers to both unboosted ATV and PIs boosted with either RTV or COBI, except the PIs noted below. For interactions between ARV agents and for dosing recommendations, refer to Tables [19c](#), [20a](#), and [20b](#).

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

**Note:** FPV, IDV, NFV, and SQV 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.

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia</b>			
Alfuzosin	All PIs	↑ alfuzosin expected	<b>Contraindicated.</b>
Doxazosin	All PIs	↑ doxazosin possible	Initiate doxazosin at lowest dose and titrate while monitoring for clinical response/toxicity. Dose reduction may be necessary.
Tamsulosin	All PIs	↑ tamsulosin expected	<b>Coadministration is not recommended.</b> If coadministered, monitor for tamsulosin toxicities.
Terazosin	All PIs	↔ or ↑ terazosin possible	Initiate terazosin at lowest dose and titrate while monitoring for clinical response/toxicity. Dose reduction may be necessary.
Silodosin	All PIs	↑ silodosin expected	<b>Contraindicated.</b>
<b>Acid Reducers</b>			
Antacids	ATV, ATV/c, ATV/r	When given simultaneously, ↓ ATV expected	Give ATV at least 2 hours before or 1–2 hours after antacids or buffered medications.
	TPV/r	TPV AUC ↓ 27%	Give TPV at least 2 hours before or 1 hour after antacids.
H2 Receptor Antagonists	ATV (unboosted)	↓ ATV	H2 receptor antagonist single dose should not exceed a dose equivalent to famotidine 20 mg, and the total daily dose should not exceed a dose equivalent to famotidine 20 mg BID in PI-naïve patients. Unboosted ATV plus famotidine should not be used in combination in PI-experienced patients.  Give ATV at least 2 hours before and at least 10 hours after the H2 receptor antagonist.
	ATV/c, ATV/r	↓ ATV	H2 receptor antagonist dose should not exceed a dose equivalent to famotidine 40 mg BID in ART-naïve patients or famotidine 20 mg BID 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 H2 receptor antagonist.  If using TDF and H2 receptor antagonist in ART-experienced patients, use ATV 400 mg plus (COBI 150 mg or RTV 100 mg).
	DRV/c, DRV/r, LPV/r	↔ demonstrated or expected	No dose adjustment necessary.

**Table 19a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 2 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Acid Reducers, continued</b>			
<b>PPIs</b>	ATV (unboosted)	↓ ATV	<b>PPIs are not recommended in patients receiving unboosted ATV.</b> In these patients, consider alternative acid-reducing agents, RTV or COBI boosting, or alternative PIs.
	ATV/c, ATV/r	↓ ATV	PPIs should not exceed a dose equivalent to omeprazole 20 mg daily in PI-naïve patients.  PPIs should be administered at least 12 hours before ATV/c or ATV/r.  <b>PPIs are not recommended in PI-experienced patients.</b>
	DRV/c, LPV/r	↔ expected	No dose adjustment necessary.
	DRV/r	Omeprazole AUC ↓ 42%	No dose adjustment necessary. If there is a lack of symptomatic relief, increase dose to no more than omeprazole 40 mg daily.
	TPV/r	Omeprazole AUC ↓ 70%	<b>Coadministration is not recommended.</b> If coadministration is necessary, dose increases of omeprazole may be considered based on clinical response.
<b>Anticoagulants and Antiplatelets</b>			
<b>Apixaban</b>	PI/c, PI/r	↑ apixaban expected	<b>Coadministration is not recommended in patients who require apixaban 2.5 mg twice daily.</b>  In patients who require apixaban 5 mg or 10 mg twice daily, reduce apixaban dose by 50%.
<b>Betrixaban</b>	ATV/c, ATV/r, LPV/r	↑ betrixaban expected	Administer an initial single dose of betrixaban 80 mg followed by betrixaban 40 mg once daily.
	DRV/c, DRV/r	↔ betrixaban expected	No dose adjustment necessary.
	TPV/r	No data	No dosing recommendations available at this time. Consider alternative ARV or warfarin.
<b>Dabigatran</b>	ATV/c, ATV/r, LPV/r	↑ dabigatran expected  With COBI 150 mg Alone: • Dabigatran AUC ↑ 110% to 127%	Dabigatran dosing recommendation depends on indication and renal function. Refer to dabigatran dosing instructions for concomitant use with P-gp inhibitors in dabigatran prescribing information.
	DRV/c, DRV/r	↔ dabigatran expected	No dose adjustment necessary.
	TPV/r	No data	No dosing recommendations available at this time. Consider alternative ARV or warfarin.
<b>Edoxaban</b>	ATV/c, ATV/r, LPV/r	↑ edoxaban expected	<b>Stroke Prevention in Nonvalvular Atrial Fibrillation Indication:</b> • No dose adjustment necessary.  <b>Deep Venous Thrombosis and Pulmonary Embolism Indication:</b> • Administer edoxaban 30 mg once daily
	DRV/c, DRV/r	↔ edoxaban expected	No dose adjustment necessary.
	TPV/r	No data	No dosing recommendations available at this time. Consider alternative ARV or warfarin.
<b>Rivaroxaban</b>	PI/c, PI/r	↑ rivaroxaban expected	<b>Coadministration is not recommended.</b>
<b>Ticagrelor</b>	All PIs	↑ ticagrelor expected	<b>Coadministration is not recommended.</b>
<b>Vorapaxar</b>	All PIs	↑ vorapaxar expected	<b>Coadministration is not recommended.</b>

**Table 19a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 3 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Anticoagulants and Antiplatelets, continued</b>			
<b>Warfarin</b>	PI/r	↓ warfarin possible	Monitor INR closely when stopping or starting PI/c and adjust warfarin dose accordingly. If switching between RTV and COBI, the effect of COBI on warfarin is not expected to be equivalent to RTV's effect on warfarin.
	PI/c	No data	
<b>Anticonvulsants</b>			
<b>Carbamazepine</b>	ATV (unboosted)	May ↓ PI levels substantially	<b>Do not coadminister.</b> Consider alternative anticonvulsant or ARV.
	ATV/r, LPV/r, TPV/r	↑ carbamazepine possible TPV/r ↑ carbamazepine AUC 26% May ↓ PI levels substantially	Consider alternative anticonvulsant or monitor levels of both drugs and assess virologic response. <b>Do not coadminister with LPV/r once daily.</b>
	DRV/r	Carbamazepine AUC ↑ 45% DRV: no significant change	Monitor anticonvulsant level and adjust dose accordingly.
	PI/c	↑ carbamazepine possible ↓ cobicistat expected ↓ PI levels expected	<b>Contraindicated.</b>
<b>Eslicarbazepine, Oxcarbazepine</b>	All PIs	↓ PI possible	Consider alternative anticonvulsant or ARV. If coadministration is necessary, monitor for virologic response. Consider monitoring anticonvulsant and PI concentration.
<b>Ethosuximide</b>	All PIs	↑ ethosuximide possible	Clinically monitor for ethosuximide toxicities.
<b>Lamotrigine</b>	ATV (unboosted)	Lamotrigine: no effect	No dose adjustment necessary.
	ATV/r	Lamotrigine AUC ↓ 32%	A dose increase of lamotrigine may be needed; consider monitoring lamotrigine concentration or consider alternative anticonvulsant.
	LPV/r	Lamotrigine AUC ↓ 50% LPV: no significant change	
	DRV/r, TPV/r	↓ lamotrigine possible	
PI/c	No data	<b>Monitor anticonvulsant level and adjust dose accordingly.</b>	
<b>Phenobarbital</b>	PI/c	↓ cobicistat expected ↓ PI levels expected	<b>Contraindicated.</b>
	ATV (unboosted), PI/r	May ↓ PI levels substantially	Consider alternative anticonvulsant or monitor levels of both drugs and assess virologic response. <b>Do not coadminister with LPV/r once daily or unboosted ATV.</b>

**Table 19a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 4 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Anticonvulsants, continued</b>			
<b>Phenytoin</b>	ATV (unboosted)	May ↓ PI levels substantially	<b>Do not coadminister.</b> Consider alternative anticonvulsant or ATV/r.
	ATV/r, DRV/r, TPV/r	↓ phenytoin possible ↓ PI possible	Consider alternative anticonvulsant or monitor levels of both drugs and assess virologic response.
	LPV/r	Phenytoin AUC ↓ 31% LPV/r AUC ↓ 33%	Consider alternative anticonvulsant or monitor levels of both drugs and assess virologic response. <b>Do not coadminister with LPV/r once daily.</b>
	PI/c	↓ cobicistat expected ↓ PI levels expected	<b>Contraindicated.</b>
<b>Valproic Acid (VPA)</b>	PI/c, PI/r	↓ or ↔ VPA possible LPV AUC ↑ 75%	Monitor VPA levels and virologic response. Monitor for LPV-related toxicities.
<b>Antidepressants, Anxiolytics, and Antipsychotics (also see Sedative/Hypnotics section below)</b>			
<b>Aripiprazole</b>	PI/c, PI/r	↑ aripiprazole expected	Administer 25% of the usual aripiprazole dose. Titrate dose based on clinical monitoring for efficacy/toxicity. Refer to aripiprazole label for doses to use in patients who have major depressive disorder or who are known to be CYP2D6 poor metabolizers.
	ATV (unboosted)	↑ aripiprazole expected	Administer 50% of the usual aripiprazole dose. Titrate based on clinical monitoring for efficacy/toxicity. Refer to aripiprazole label for doses to use in patients who have major depressive disorder or who are known to be CYP2D6 poor metabolizers.
<b>Brexpiprazole</b>	PI/c, PI/r	↑ brexpiprazole expected	Administer 25% of the usual brexpiprazole dose. Titrate based on clinical monitoring for efficacy/toxicity. Refer to brexpiprazole label for doses to use in patients who have major depressive disorder or who are known to be CYP2D6 poor metabolizers.
	ATV (unboosted)	↑ brexpiprazole expected	Administer 50% of the usual brexpiprazole dose. Titrate based on clinical monitoring for efficacy/toxicity. Refer to brexpiprazole label for doses to use in patients who have major depressive disorder or who are known to be CYP2D6 poor metabolizers.
<b>Bupropion</b>	LPV/r	Bupropion AUC ↓ 57%	Titrate bupropion dose based on clinical response.
	TPV/r	Bupropion AUC ↓ 46%	
	ATV/r, DRV/r	↓ bupropion possible	<b>No dose adjustment necessary.</b>
	PI/c	↔ bupropion expected	
<b>Buspirone</b>	All PIs	↑ buspirone expected	Use a low dose of buspirone with caution and titrate buspirone dose based on clinical response.



**Table 19a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 5 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Antidepressants, Anxiolytics, and Antipsychotics (also see Sedative/Hypnotics section below), continued</b>			
<b>Cariprazine</b>	All PIs	↑ cariprazine expected	<p><u>Starting Cariprazine in a Patient Already Receiving a PI:</u></p> <ul style="list-style-type: none"> <li>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.</li> </ul> <p><u>Starting a PI in a Patient Already Receiving Cariprazine:</u></p> <ul style="list-style-type: none"> <li>For patients receiving cariprazine 3 mg or cariprazine 6 mg daily, reduce dose by half. For patients taking cariprazine 4.5 mg daily, the dose should be reduced to cariprazine 1.5 mg or cariprazine 3 mg daily. For patients taking cariprazine 1.5 mg daily, change to cariprazine 1.5 mg every other day. If PI is withdrawn, cariprazine dose may need to be increased.</li> </ul>
<b>Fluvoxamine</b>	All PIs	↑ fluvoxamine possible	<b>Titrate fluvoxamine dose based on clinical response.</b>
<b>Lurasidone</b>	PI/c, PI/r	↑ lurasidone expected	<b>Contraindicated.</b> Consider alternative therapy. If coadministration is necessary, reduce lurasidone dose by 50%.
	ATV (unboosted)	↑ lurasidone expected	
<b>Pimavanserin</b>	All PIs	↑ pimavanserin expected	<b>Reduce dose from pimavanserin 34 mg daily to pimavanserin 17 mg daily.</b>
<b>Pimozide</b>	All PIs	↑ pimozide expected	<b>Contraindicated.</b>
<b>Quetiapine</b>	All PIs	↑ quetiapine expected	<p><u>Starting Quetiapine in a Patient Receiving a PI:</u></p> <ul style="list-style-type: none"> <li>Start quetiapine at the lowest dose and titrate up as needed. Monitor for quetiapine effectiveness and adverse effects.</li> </ul> <p><u>Starting a PI in a Patient Receiving a Stable Dose of Quetiapine:</u></p> <ul style="list-style-type: none"> <li>Reduce quetiapine dose to 1/6 of the original dose. Closely monitor for quetiapine effectiveness and adverse effects.</li> </ul>
<b>Trazodone</b>	All PIs	RTV 200 mg BID (for 2 days) ↑ trazodone AUC 240%	Use lowest dose of trazodone and monitor for CNS and CV adverse effects.
<b>Tricyclic Antidepressants (TCA)</b> Amitriptyline, desipramine, doxepin, imipramine, nortriptyline	All PIs	↑ TCA expected	Use lowest possible TCA dose and titrate based on clinical assessment and/or drug levels.
<b>Other Antipsychotics (CYP3A4 and/or CYP2D6 substrates)</b>	PI/c, PI/r	↑ antipsychotic possible	Titrate antipsychotic dose using the lowest initial dose, or adjust maintenance dose accordingly. Monitor for toxicities.
<b>Other Selective Serotonin Reuptake Inhibitors (SSRIs)</b> (e.g., citalopram, escitalopram, fluoxetine, paroxetine, sertraline)	DRV/r	Paroxetine AUC ↓ 39% Sertraline AUC ↓ 49%	Titrate SSRI dose based on clinical response.
	ATV/r, LPV/r, TPV/r	No data	
	PI/c	Effects unknown	Titrate SSRI dose using the lowest available initial or maintenance dose.

**Table 19a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 6 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Antifungals</b>			
<b>Fluconazole</b>	PI/c, ATV/r, DRV/r, LPV/r	No significant effect observed or expected	No dose adjustment necessary.
	TPV/r	TPV AUC ↑ 50%	Fluconazole >200 mg daily is not recommended. If high-dose fluconazole is indicated, consider alternative ARV.
<b>Isavuconazole</b>	LPV/r	Isavuconazole AUC ↑ 96% LPV AUC ↓ 27% RTV AUC ↓ 31%	If coadministered, consider monitoring isavuconazole concentrations and toxicities and assessing virologic response.
	All PIs except LPV/r	↑ isavuconazole possible ↑ or ↓ PI possible	If coadministered, consider monitoring isavuconazole concentrations and toxicities. Monitor for PI toxicity and virologic response.
<b>Itraconazole</b>	All PIs	↑ itraconazole possible ↑ PI possible	Consider monitoring itraconazole level to guide dose adjustments. Doses >200 mg/day <b>are not recommended</b> with PI/r, ATV/c, or DRV/c unless dosing is guided by itraconazole levels.
<b>Posaconazole</b>	ATV/r	ATV AUC ↑ 146% ↑ posaconazole possible	If coadministered, monitor for PI adverse effects. Consider monitoring for posaconazole concentrations and toxicities.
	ATV	ATV AUC ↑ 268% ↑ posaconazole possible	
	ATV/c, DRV/c, DRV/r, LPV/r, TPV/r	↑ PI possible ↑ posaconazole possible	
<b>Voriconazole</b>	ATV (unboosted)	↑ voriconazole possible ↑ PI possible	Monitor for toxicities.
	All PI/r	RTV 100 mg BID ↓ voriconazole AUC 39%	Do not coadminister voriconazole and RTV or COBI unless benefit outweighs risk. If coadministered, consider monitoring voriconazole concentration and adjust dose accordingly.
	PI/c	Effect on voriconazole unknown	
<b>Antihyperglycemics</b>			
<b>Canagliflozin</b>	PI/r	↓ canagliflozin expected	If a patient is already tolerating canagliflozin 100 mg daily, has an eGFR >60 mL/min/1.73m <sup>2</sup> , and requires additional glycemic control, consider increasing dose to canagliflozin 300 mg daily.
	PI/c	↓ canagliflozin possible	If used in combination, monitor glycemic control.
<b>Saxagliptin</b>	All PIs	↑ saxagliptin expected	Limit saxagliptin dose to 2.5 mg once daily
<b>Dapagliflozin/Saxagliptin</b>	All PIs	↑ saxagliptin expected	<b>Do not coadminister</b> , as this coformulated drug contains 5 mg of saxagliptin.
<b>Antimalarials</b>			
<b>Artemether/Lumefantrine</b>	DRV/r	Artemether AUC ↓ 16% DHA <sup>a</sup> AUC ↓ 18% Lumefantrine AUC ↑ 2.5-fold	Clinical significance unknown. If used, monitor closely for antimalarial efficacy and lumefantrine toxicity.
	DRV/c	↑ lumefantrine expected Effect on artemether unknown	
	LPV/r	Artemether AUC ↓ 40% DHA AUC ↓ 17% Lumefantrine AUC ↑ 470%	

**Table 19a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 7 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Antimalarials, continued</b>			
<b>Artesunate/Mefloquine</b>	LPV/r	Dihydroartemisinin AUC ↓ 49% Mefloquine AUC ↓ 28% ↔ LPV	Clinical significance unknown. If used, monitor closely for antimalarial efficacy.
<b>Atovaquone/Proguanil</b>	ATV/r, LPV/r	<u>With ATV/r:</u> • Atovaquone AUC ↓ 46% • Proguanil AUC ↓ 41% <u>With LPV/r:</u> • Atovaquone AUC ↓ 74% • Proguanil AUC ↓ 38%	No dose recommendation. Consider alternative drug for malaria prophylaxis, if possible.
<b>Mefloquine</b>	RTV	<u>With RTV 200 mg BID:</u> • RTV AUC ↓ 31%, C <sub>min</sub> ↓ 43% ↔ mefloquine	Use with caution. Effect on exposure of RTV-boosted PIs is unknown.
<b>Antimycobacterials (for treatment of <i>Mycobacterium tuberculosis</i> and nontuberculosis mycobacterial infections)</b>			
<b>Bedaquiline</b>	All PIs	<u>With LPV/r:</u> • Bedaquiline AUC ↑ 1.9-fold <u>With Other PI/r, ATV/c, or DRV/c:</u> • ↑ bedaquiline possible	Clinical significance unknown. Use with caution if benefit outweighs the risk and monitor for QTc prolongation and liver function tests.
<b>Clarithromycin</b>	ATV (unboosted)	Clarithromycin AUC ↑ 94%	May cause QTc prolongation. Reduce clarithromycin dose by 50%. Consider alternative therapy (e.g., azithromycin).
	All PIs	↑ clarithromycin expected DRV/r ↑ clarithromycin AUC 57% LPV/r ↑ clarithromycin expected RTV 500 mg BID ↑ clarithromycin 77% TPV/r ↑ clarithromycin 19% Clarithromycin ↑ TPV 66%	Consider alternative macrolide (e.g., azithromycin). Monitor for clarithromycin-related toxicities or consider an alternative macrolide (e.g., azithromycin). Reduce clarithromycin dose by 50% in patients with CrCl 30–60 mL/min. Reduce clarithromycin dose by 75% in patients with CrCl <30 mL/min.

**Table 19a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 8 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Antimycobacterials (for treatment of <i>Mycobacterium tuberculosis</i> and nontuberculosis mycobacterial infections), continued</b>			
<b>Rifabutin</b>	ATV (unboosted)	↑ rifabutin AUC expected	Rifabutin 150 mg once daily or 300 mg three times a week.
	ATV/r	Compared with Rifabutin (300 mg Once Daily) Alone, Rifabutin (150 mg Once Daily) plus ATV/r: • Rifabutin AUC ↑ 110% and metabolite AUC ↑ 2,101%	Monitor for antimycobacterial activity and consider therapeutic drug monitoring.  PK data reported in this table are results from healthy volunteer studies. Lower rifabutin exposure has been reported in patients with HIV than in healthy study participants.
	DRV/r	Compared with Rifabutin (300 mg Once Daily) Alone, Rifabutin (150 mg Every Other Day) plus DRV/r: • Rifabutin AUC ↔ and metabolite AUC ↑ 881%	
	LPV/r	Compared with Rifabutin (300 mg daily) Alone, Rifabutin (150 mg Once Daily) plus LPV/r: • Rifabutin AUC ↑ 203% and metabolite AUC ↑ 375%	
	TPV/r	Rifabutin AUC ↑ 190% and metabolite AUC ↑ 1,971%	
	PI/c	↑ rifabutin expected	
<b>Rifampin</b>	All PIs	↓ PI concentration by >75%	<b>Contraindicated.</b> Additional RTV does not overcome this interaction and may increase hepatotoxicity. Additional COBI is not recommended. Consider rifabutin if a rifamycin is indicated.
<b>Rifapentine</b>	All PIs	↓ PI expected	<b>Do not coadminister.</b>
<b>Antipneumocystis and Antitoxoplasmosis Drug</b>			
<b>Atovaquone</b>	ATV/r	↔ atovaquone	No dose adjustment necessary.
<b>Cardiac Medications</b>			
<b>Amiodarone</b>	TPV/r	↑ both amiodarone and PI possible	<b>Contraindicated.</b>
	All PIs except TPV/r	↑ both amiodarone and PI possible	Use with caution. Monitor for amiodarone toxicity and consider ECG and amiodarone drug levels.
<b>Antiarrhythmics</b> (e.g., disopyramide, dofetilide, lidocaine, mexiletine, propafenone)	ATV (unboosted)	↑ antiarrhythmic possible	Consider alternative antiarrhythmics or ARV. If coadministered, monitor for antiarrhythmic toxicities.
	PI/c, PI/r	↑ antiarrhythmic possible	<b>Do not coadminister.</b> Consider alternative antiarrhythmics or ARV.
<b>Dronedarone</b>	ATV (unboosted)	↑ dronedarone possible	<b>Do not coadminister.</b>
	PI/c, PI/r	↑ dronedarone expected	<b>Contraindicated.</b>
<b>Flecainide</b>	All PIs except TPV/r	↑ flecainide possible	<b>Do not coadminister.</b>
	TPV/r	↑ flecainide expected	<b>Contraindicated.</b>

**Table 19a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 9 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Cardiac Medications, continued</b>			
<b>Propafenone</b>	All PIs except TPV/r	↑ propafenone possible	<b>Do not coadminister.</b>
	TPV/r	↑ propafenone expected	<b>Contraindicated.</b>
<b>Quinidine</b>	All PIs except TPV/r	↑ quinidine possible	<b>Do not coadminister.</b>
	TPV/r	↑ quinidine expected	<b>Contraindicated.</b>
<b>Beta-Blockers</b> (e.g., carvedilol, metoprolol, timolol)	All PIs	↑ beta-blockers possible	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).
<b>Bosentan</b>	All PIs	LPV/r ↑ bosentan 48-fold (Day 4) and 5-fold (Day 10) ↓ ATV expected	<b>Do not coadminister bosentan and unboosted ATV.</b> <u>In Patients on a PI (Other than Unboosted ATV) &gt;10 Days:</u> • Start bosentan at 62.5 mg once daily or every other day. <u>In Patients on Bosentan who Require a PI (Other than Unboosted ATV):</u> • 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. <u>When Switching Between COBI and RTV:</u> • Maintain same bosentan dose.
<b>Calcium Channel Blockers (CCBs), Except Diltiazem</b>	All PIs	↑ dihydropyridine possible ↑ verapamil possible	Use with caution. Titrate CCB dose and monitor closely. ECG monitoring is recommended when CCB is used with ATV.
<b>Digoxin</b>	PI/c, PI/r	RTV (200 mg BID) ↑ digoxin AUC 29% and ↑ half-life 43% DRV/r ↑ digoxin AUC 36% COBI ↑ digoxin C <sub>max</sub> 41% and ↔ AUC	Use with caution. Monitor digoxin levels. Digoxin dose may need to be decreased. Titrate initial digoxin dose.
<b>Diltiazem</b>	ATV/c, ATV/r, ATV (unboosted)	Unboosted ATV ↑ diltiazem AUC 125% Greater ↑ likely with ATV/c or ATV/r	Decrease diltiazem dose by 50%. ECG monitoring is recommended.
	DRV/c, DRV/r, LPV/r, TPV/r	↑ diltiazem possible	Use with caution. Adjust diltiazem according to clinical response and toxicities.
<b>Eplerenone</b>	PI/c, PI/r	↑ eplerenone expected	<b>Contraindicated.</b>
<b>Ranolazine</b>	ATV (unboosted)	↑ ranolazine possible	<b>Do not coadminister.</b>
	PI/c, PI/r	↑ ranolazine expected	<b>Contraindicated.</b>
<b>Ivabradine</b>	All PIs	↑ ivabradine expected	<b>Contraindicated.</b>

**Table 19a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 10 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Corticosteroids</b>			
<b>Beclomethasone</b> Inhaled or intranasal	DRV/r	↔ 17-BMP (active metabolite) AUC  RTV 100 mg BID ↑ 17-BMP AUC 2-fold	No dose adjustment necessary.
	All PIs except DRV/r	↔ expected	No dose adjustment necessary.
<b>Budesonide, Ciclesonide, Fluticasone, Mometasone</b> Inhaled or intranasal	All PIs	↑ glucocorticoids possible  RTV 100 mg BID ↑ fluticasone AUC 350-fold	Coadministration can result in adrenal insufficiency and Cushing's syndrome. <b>Do not coadminister unless potential benefits of inhaled or intranasal corticosteroid outweigh the risks of adverse effects associated with corticosteroids.</b> Consider an alternative corticosteroid (e.g., beclomethasone).
<b>Betamethasone, Budesonide</b> Systemic	All PIs	↑ glucocorticoids possible  ↓ PI possible	Coadministration can result in adrenal insufficiency and Cushing's syndrome. <b>Do not coadminister unless potential benefits of systemic corticosteroid outweigh the risks of adverse effects associated with systemic corticosteroids.</b>
<b>Dexamethasone</b> Systemic	All PIs	↑ glucocorticoids possible  ↓ PI possible	Consider alternative corticosteroid for long-term use. If coadministration is necessary, monitor virologic response to ART.
<b>Prednisone, Prednisolone</b> Systemic	LPV/r	↑ prednisolone AUC 31%	Coadministration may be considered if the potential benefits outweigh the risks of adverse effects associated with systemic corticosteroids. If coadministered, monitor for adrenal insufficiency, Cushing's syndrome, and other corticosteroid-associated toxicities.
	All PIs	↑ prednisolone possible	
<b>Betamethasone, Methylprednisolone, Triamcinolone</b> Local injections, including intra-articular, epidural, or intra-orbital	All PIs	↑ glucocorticoids expected	<b>Do not coadminister.</b> Coadministration can result in adrenal insufficiency and Cushing's syndrome.
<b>Hepatitis C Direct-Acting Antiviral Agents</b>			
<b>Daclatasvir</b>	ATV/c, ATV/r	↑ daclatasvir	Decrease daclatasvir dose to 30 mg once daily.
	ATV (unboosted), DRV/c, DRV/r, LPV/r	↔ daclatasvir	No dose adjustment necessary.
	TPV/r	No data	No dosing recommendations available at this time.
<b>Dasabuvir plus Paritaprevir/Ombitasvir/RTV</b>	ATV (unboosted)	↔ ATV	ATV 300 mg alone, <b>without COBI or additional RTV</b> , should be given in the morning with dasabuvir plus paritaprevir/ombitasvir/RTV.
	DRV	DRV C <sub>min</sub> ↓ 43% to 48%	<b>Do not coadminister.</b>
	LPV/r	Paritaprevir AUC ↑ 117%	<b>Do not coadminister.</b>
	ATV/c, DRV/c, TPV/r	No data	<b>Do not coadminister.</b>

**Table 19a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 11 of 19)

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

**Table 19a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 12 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Hepatitis C Direct-Acting Antiviral Agents, continued</b>			
Simeprevir	All PIs	Compared with Simeprevir 150 mg Alone. Simeprevir 50 mg plus DRV/r 800 mg/100 mg Daily: • Simeprevir AUC ↑ 159%  RTV 100 mg BID ↑ simeprevir AUC 618%	<b>Do not coadminister.</b>
Sofosbuvir	TPV/r	↓ sofosbuvir expected	<b>Do not coadminister.</b>
Sofosbuvir/ Velpatasvir	ATV/r	↔ ATV/r ↔ sofosbuvir Velpatasvir AUC ↑ 2.4-fold	No dose adjustment necessary.
	DRV/r	↔ DRV/r Sofosbuvir AUC ↓ 28% ↔ velpatasvir	No dose adjustment necessary.
	ATV (unboosted), ATV/c, DRV/c, LPV/r	↔ sofosbuvir and velpatasvir expected	No dose adjustment necessary.
	TPV/r	↓ sofosbuvir expected ↓ velpatasvir expected	<b>Do not coadminister.</b>
Sofosbuvir/ Velpatasvir/ Voxilaprevir	ATV (unboosted), ATV/c, ATV/r	<u>When Given with ATV/r:</u> • Voxilaprevir AUC ↑ 4.3-fold • Velpatasvir AUC ↑ 93% • Sofosbuvir AUC ↑ 40%	<b>Do not coadminister.</b>
	LPV/r	↑ voxilaprevir expected	<b>Do not coadminister.</b>
	DRV/c, DRV/r	<u>When Given with DRV/r:</u> • Voxilaprevir AUC ↑ 2.4-fold • ↔ DRV/r, velpatasvir, and sofosbuvir	No dose adjustment needed.
	TPV/r	↓ sofosbuvir expected ↓ velpatasvir expected Effect on voxilaprevir is unknown.	<b>Do not coadminister.</b>
<b>Herbal Products</b>			
St. John's Wort	All PIs	↓ PI expected	<b>Contraindicated.</b>



**Table 19a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 13 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Hormonal Therapies</b>			
<b>Hormonal Contraceptives Oral</b>	ATV (unboosted)	Ethinyl estradiol AUC ↑ 48% Norethindrone AUC ↑ 110%	Prescribe oral contraceptive that contains no more than 30 mcg of ethinyl estradiol <sup>b</sup> or recommend alternative contraceptive method.  Oral contraceptives containing less than 25 mcg of ethinyl estradiol or progestins other than norethindrone or norgestimate have not been studied.
	ATV/r	Ethinyl estradiol AUC ↓ 19% and C <sub>min</sub> ↓ 37% Norgestimate ↑ 85% Norethindrone AUC ↑ 51% and C <sub>min</sub> ↑ 67%	Oral contraceptive should contain at least 35 mcg of ethinyl estradiol. <sup>c</sup>  Oral contraceptives containing progestins other than norethindrone or norgestimate have not been studied.
	ATV/c	Drospirenone AUC ↑ 2.3-fold Ethinyl estradiol AUC ↓ 22%	<b>Contraindicated with drospirenone-containing hormonal contraceptive due to potential for hyperkalemia.</b> Consider alternative or additional contraceptive method or alternative ARV drug.
	DRV/c	Drospirenone AUC ↑ 1.6-fold Ethinyl estradiol AUC ↓ 30%	Clinical monitoring is recommended due to the potential for hyperkalemia. Consider alternative or additional contraceptive method or alternative ARV.
	DRV/r, LPV/r, TPV/r	Ethinyl estradiol AUC ↓ 37% to 55% Norethindrone AUC ↓ 14% to 34% <u>With TPV/r:</u> • ↔ norethindrone AUC	Consider alternative or additional contraceptive method or alternative ARV drug.
<b>Depot MPA Injectable</b>	LPV/r	MPA AUC ↑ 46% No significant change in C <sub>min</sub>	No dose adjustment necessary.
<b>Etonogestrel-Releasing Subdermal Implant</b>	LPV/r	Etonogestrel AUC ↑ 52% and C <sub>min</sub> ↑ 34%	Use standard dose.
	All other PIs	No data	Consider alternative or additional contraceptive method or alternative ARV drug.
<b>Etonogestrel/Ethinyl Estradiol Vaginal Ring</b>	ATV/r	Ethinyl estradiol AUC ↓ 26% Etonogestrel AUC ↑ 79%	Use standard dose.
<b>Transdermal Ethinyl Estradiol/Norelgestromin</b>	LPV/r	↔ LPV Ethinyl estradiol AUC ↓ 45%, norelgestromin AUC ↑ 83%	Use standard dose.
	All other PIs	No data	Consider alternative or additional contraceptive method or alternative ARV drug.

**Table 19a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 14 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Hormonal Therapies, continued</b>			
<b>Menopausal Hormone Replacement Therapy (HRT)</b>	All PIs	↓ estrogen possible with estradiol or conjugated estrogen (equine and synthetic)	Adjust estrogen dosage as needed based on clinical effects.
	All PIs	↑ drospirenone possible ↑ medroxyprogesterone ↑ micronized progesterone See Hormonal Contraceptives for other progestin-PI interactions	Adjust progestin/progesterone dosage as needed based on clinical effects. Because drospirenone is prescribed as a lower dose for menopausal HRT than the products used for hormonal contraceptives, it is not contraindicated with ATV/c products.
<b>Gender-Affirming Hormone Therapy</b>	All PIs	↓ estradiol possible	Adjust estradiol dosage as needed based on clinical effects and endogenous hormone concentrations.
	All PIs	↔ finasteride, goserelin, leuprolide acetate, and spironolactone expected	No dose adjustment necessary.
	All PIs	↑ dutasteride possible	Adjust dutasteride dosage as needed based on clinical effects and endogenous hormone concentrations.
	All PIs	↓ testosterone possible	Adjust testosterone dosage as needed based on clinical effects and endogenous hormone concentrations.
<b>HMG-CoA Reductase Inhibitors</b>			
<b>Atorvastatin</b>	ATV (unboosted), ATV/r	↑ atorvastatin possible	Titrate atorvastatin dose carefully and use lowest dose necessary while monitoring for toxicities.
	ATV/c	Atorvastatin AUC ↑ 9.2-fold, C <sub>max</sub> ↑ 18.9-fold	<b>Coadministration is not recommended.</b>
	DRV/r	DRV/r plus atorvastatin 10 mg similar to atorvastatin 40 mg administered alone	Titrate atorvastatin dose carefully and use the lowest dose necessary while monitoring for toxicities. Do not exceed 20 mg atorvastatin daily.
	DRV/c	Atorvastatin AUC ↑ 3.9-fold, C <sub>max</sub> ↑ 4.2-fold	Titrate atorvastatin dose carefully and use lowest dose necessary while monitoring for toxicities. Do not exceed 20 mg atorvastatin daily.
	LPV/r	Atorvastatin AUC ↑ 5.9-fold, C <sub>max</sub> ↑ 4.7-fold	Titrate atorvastatin dose carefully and use lowest dose necessary while monitoring for toxicities. Do not exceed 20 mg atorvastatin daily.
	TPV/r	Atorvastatin AUC ↑ 9.4-fold, C <sub>max</sub> ↑ 8.6-fold	<b>Do not coadminister.</b>
<b>Lovastatin</b>	All PIs	Significant ↑ lovastatin expected	<b>Contraindicated.</b>
<b>Pitavastatin</b>	All PIs	ATV ↑ pitavastatin AUC 31% and C <sub>max</sub> ↑ 60% ↔ ATV DRV/r ↓ pitavastatin AUC 26% ↔ DRV/r LPV/r ↓ pitavastatin AUC 20% ↔ LPV	No dose adjustment necessary.

**Table 19a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 15 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>HMG-CoA Reductase Inhibitors, continued</b>			
<b>Pravastatin</b>	ATV/c, ATV/r	No data	Titrate pravastatin dose carefully while monitoring for toxicities.
	DRV/c, DRV/r	<b>With DRV/r:</b> • Pravastatin AUC ↑ 81% following single dose of pravastatin • Pravastatin AUC ↑ 23% at steady state	Titrate pravastatin dose carefully while monitoring for toxicities.
	LPV/r	Pravastatin AUC ↑ 33%	No dose adjustment necessary.
<b>Rosuvastatin</b>	ATV/r	Rosuvastatin AUC ↑ 3-fold, C <sub>max</sub> ↑ 7-fold	Titrate rosuvastatin dose carefully and use lowest dose necessary while monitoring for toxicities. Do not exceed rosuvastatin 10 mg daily.
	ATV/c	Rosuvastatin AUC ↑ 3.4-fold, C <sub>max</sub> ↑ 10.6-fold	
	DRV/c	Rosuvastatin AUC ↑ 1.9-fold, C <sub>max</sub> ↑ 3.8-fold	Titrate rosuvastatin dose carefully and use the lowest dose necessary while monitoring for toxicities. Do not exceed rosuvastatin 20 mg daily.
	DRV/r	Rosuvastatin AUC ↑ 48%, C <sub>max</sub> ↑ 2.4-fold	Titrate rosuvastatin dose carefully and use the lowest necessary dose while monitoring for toxicities.
	LPV/r	Rosuvastatin AUC ↑ 2.1-fold, C <sub>max</sub> ↑ 4.7-fold	Titrate rosuvastatin dose carefully and use the lowest necessary dose. Do not exceed rosuvastatin 10 mg daily.
	TPV/r	Rosuvastatin AUC ↑ 26%, C <sub>max</sub> ↑ 2.2-fold	No dose adjustment necessary.
<b>Simvastatin</b>	All PIs	Significant ↑ simvastatin expected	<b>Contraindicated.</b>
<b>Immunosuppressants</b>			
<b>Cyclosporine, Everolimus, Sirolimus, Tacrolimus</b>	All PIs	↑ immunosuppressant expected	Initiate with an adjusted dose of immunosuppressant to account for potential increased concentrations of the immunosuppressant and monitor for toxicities. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with specialist as necessary.

**Table 19a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 16 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Narcotics and Treatment for Opioid Dependence</b>			
<b>Buprenorphine</b> Sublingual, buccal, or implant	ATV (unboosted)	Buprenorphine AUC ↑ 93% Norbuprenorphine <sup>d</sup> AUC ↑ 76% ↓ ATV possible	<b>Do not coadminister.</b>
	ATV/r	Buprenorphine AUC ↑ 66% Norbuprenorphine <sup>d</sup> AUC ↑ 105%	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.
	DRV/r	No significant effect on buprenorphine Norbuprenorphine <sup>d</sup> AUC ↑ 46% and C <sub>min</sub> ↑ 71%	No dose adjustment necessary. Clinical monitoring is recommended. When transferring buprenorphine from transmucosal delivery to implantation, monitor to ensure buprenorphine effect is adequate and not excessive.
	LPV/r	No significant effect	
	TPV/r	No significant effect on buprenorphine Norbuprenorphine <sup>d</sup> AUC, C <sub>max</sub> <sup>1</sup> and C <sub>min</sub> ↓ 80% TPV C <sub>min</sub> ↓ 19% to 40%	Consider monitoring TPV level. When transferring buprenorphine from transmucosal delivery to implantation, monitor to ensure buprenorphine effect is adequate and not excessive.
	PI/c	Effects unknown	Titrate buprenorphine dose using the lowest initial dose. Dose adjustment of buprenorphine may be needed. It may be necessary to remove implant and treat with a formulation that permits dose adjustments. Clinical monitoring is recommended.
<b>Fentanyl</b>	All PIs	↑ fentanyl possible	Clinical monitoring is recommended, including for potentially fatal respiratory depression.
<b>Methadone</b>	ATV (unboosted)	No significant effect	No dose adjustment necessary.
	PI/c	Effects unknown	Titrate methadone dose using the lowest feasible initial dose. Dose adjustment of methadone may be needed. Clinical monitoring is recommended.
	All PI/r	ATV/r and DRV/r ↓ R-methadone <sup>e</sup> AUC 16% to 18% LPV/r ↓ methadone AUC 26% to 53% TPV/r ↓ R-methadone <sup>e</sup> AUC 48%	Opioid withdrawal is unlikely but may occur. Dosage adjustment of methadone is not usually required, but monitor for opioid withdrawal and increase methadone dose as clinically indicated.
<b>Oxycodone</b>	All PIs	Oxycodone AUC ↑ 2.6-fold with LPV/r	Monitor for opioid-related adverse effects. Oxycodone dose reduction may be necessary.
<b>Tramadol</b>	All PIs	↑ tramadol possible	Tramadol dose reduction may be necessary. Monitor for tramadol toxicities and clinical response.

**Table 19a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 17 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>PDE5 Inhibitors</b>			
Avanafil	All PIs except unboosted ATV	RTV (600 mg BID for 5 days) ↑ avanafil AUC 13-fold and ↑ C <sub>max</sub> 2.4-fold	<b>Coadministration is not recommended.</b>
	ATV (unboosted)	No data	Avanafil dose should not exceed 50 mg once every 24 hours.
Sildenafil	All PIs	DRV/r plus sildenafil 25 mg similar to sildenafil 100 mg alone RTV 500 mg BID ↑ sildenafil AUC 1,000%	<u>For Treatment of Erectile Dysfunction:</u> • Start with sildenafil 25 mg every 48 hours and monitor for adverse effects of sildenafil. <u>For Treatment of PAH:</u> • <b>Contraindicated.</b>
Tadalafil	All PIs	RTV 200 mg BID ↑ tadalafil AUC 124% TPV/r (1st dose) ↑ tadalafil AUC 133% No significant effect on TPV/r steady state	<u>For Treatment of Erectile Dysfunction:</u> • Start with tadalafil 5-mg dose and do not exceed a single dose of tadalafil 10 mg every 72 hours. Monitor for adverse effects of tadalafil. <u>For Treatment of PAH</u> <i>In Patients on a PI &gt;7 Days:</i> • Start with tadalafil 20 mg once daily and increase to tadalafil 40 mg once daily based on tolerability. <i>In Patients on Tadalafil who Require a PI:</i> • Stop tadalafil ≥24 hours before PI initiation. Seven days after PI initiation, restart tadalafil at 20 mg once daily and increase to tadalafil 40 mg once daily based on tolerability. <i>In Patients Switching between COBI and RTV:</i> • Maintain tadalafil dose. <u>For Treatment of Benign Prostatic Hyperplasia:</u> • Maximum recommended daily dose is tadalafil 2.5 mg per day.
Vardenafil	All PIs	RTV 600 mg BID ↑ vardenafil AUC 49-fold	Start with vardenafil 2.5 mg every 72 hours and monitor for adverse effects of vardenafil.
<b>Sedative/Hypnotics</b>			
Alprazolam, Clonazepam, Diazepam	All PIs	↑ benzodiazepine possible RTV (200 mg BID for 2 days) ↑ alprazolam half-life 222% and ↑ AUC 248%	Consider alternative benzodiazepines, such as lorazepam, oxazepam, or temazepam.
Lorazepam, Oxazepam, Temazepam	All PIs	No data	These benzodiazepines are metabolized via non-CYP450 pathways; thus, there is less interaction potential than with other benzodiazepines.
Midazolam	All PIs	↑ midazolam expected	<b>Oral midazolam is contraindicated with PIs.</b>  Parenteral midazolam can be used with caution when given as a single dose in a monitored situation for procedural sedation.
Suvorexant	All PIs	↑ suvorexant expected	<b>Coadministration is not recommended.</b>

**Table 19a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 18 of 19)

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Sedative/Hypnotics, continued</b>			
Triazolam	All PIs	↑ triazolam expected RTV (200 mg BID) ↑ triazolam half-life 1,200% and AUC 2,000%	<b>Contraindicated.</b>
Zolpidem	PI/c, PI/r	↑ zolpidem possible	Initiate zolpidem at a low dose. Dose reduction may be necessary.
<b>Miscellaneous Drugs</b>			
Calcifediol	All PIs	↑ calcifediol possible	Dose adjustment of calcifediol may be required, and serum 25-hydroxyvitamin D, intact PTH, and serum calcium concentrations should be closely monitored.
Cisapride	All PIs	↑ cisapride expected	<b>Contraindicated.</b>
Colchicine	All PIs	RTV 100 mg BID ↑ colchicine AUC 296% and C <sub>max</sub> 184%  Significant ↑ colchicine expected with all PIs, with or without COBI or RTV	<u>For Treatment of Gout Flares:</u> • 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.  <u>For Prophylaxis of Gout Flares:</u> • Administer colchicine 0.3 mg once daily or every other day.  <u>For Treatment of Familial Mediterranean Fever:</u> • Do not exceed colchicine 0.6 mg once daily or colchicine 0.3 mg BID.  <b>Do not coadminister in patients with hepatic or renal impairment.</b>
Dronabinol	All PIs	↑ dronabinol possible	Monitor for increased dronabinol-related adverse reactions.
Eluxadoline	All PIs	↑ eluxadoline expected	Administer eluxadoline at a dose of 75 mg twice daily and monitor for eluxadoline-related adverse effects.
<b>Enzalutamide</b>	<b>All PIs</b>	<b>↓ PI expected</b>	<b>Contraindicated.</b>
Ergot Derivatives	All PIs	↑ dihydroergotamine, ergotamine, methylergonovine expected	<b>Contraindicated.</b>
Flibanserin	All PIs	↑ flibanserin expected	<b>Contraindicated.</b>
Irinotecan	ATV (unboosted), ATV/c, ATV/r	↑ irinotecan expected	<b>Contraindicated.</b>
<b>Mitotane</b>	<b>All PIs</b>	<b>↓ PI expected</b>	<b>Contraindicated.</b>
Salmeterol	All PIs	↑ salmeterol possible	<b>Do not coadminister</b> because of potential increased risk of salmeterol-associated CV events.

**Table 19a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 19 of 19)

<sup>a</sup> DHA is an active metabolite of artemether.

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

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

<sup>d</sup> Norbuprenorphine is an active metabolite of buprenorphine.

<sup>e</sup> R-methadone is the active form of methadone.

**Key to Symbols:**

↑ = increase

↓ = decrease

↔ = no change

**Key to Acronyms:** 17-BMP = beclomethasone 17-monopropionate; ALT = alanine aminotransferase; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BID = twice daily; C<sub>max</sub> = maximum plasma concentration; C<sub>min</sub> = minimum plasma concentration; CNS = central nervous system; COBI = 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; FPV = fosamprenavir; 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; TDF = tenofovir disoproxil fumarate; TPV = tipranavir; TPV/r = tipranavir/ritonavir

**Table 19b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 1 of 10)**

This table provides information relating to PK interactions between NNRTIs and non-ARV drugs. For interactions between ARV agents and for dosing recommendations, refer to Tables 19c, 20a, and 20b. Recommendations for managing a particular drug interaction may differ depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or if a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly.

**Note:** DLV is **not** included in this table. Please refer to the DLV FDA package insert for information regarding drug interactions. The term “All NNRTIs” in this table refers to all NNRTIs except for DLV.

Concomitant Drug Class/ Name	NNRTI <sup>a</sup>	Effect on NNRTI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Acid Reducers</b>			
<b>Antacids</b>	RPV	↓ RPV expected when given simultaneously	Give antacids at least 2 hours before or at least 4 hours after RPV.
<b>H2 Receptor Antagonists</b>	RPV	↓ RPV	Give H2 receptor antagonists at least 12 hours before or at least 4 hours after RPV.
<b>PPIs</b>	RPV	With Omeprazole 20 mg Daily: • RPV AUC ↓ 40% and C <sub>min</sub> ↓ 33%	<b>Contraindicated. Do not coadminister.</b>
<b>Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia</b>			
<b>Alfuzosin, Doxazosin, Silodosin</b>	EFV, ETR, NVP	↓ alpha antagonist expected	Consider alternative therapy. If coadministration is necessary, monitor for therapeutic effectiveness of alpha antagonist.
<b>Tamsulosin</b>	EFV, ETR, NVP	↓ tamsulosin expected	Monitor for therapeutic effectiveness of tamsulosin after 2 to 4 weeks of dosing. May need to increase to tamsulosin 0.8 mg once daily for patients who fail to respond to the 0.4 mg dose.
<b>Anticoagulants/Antiplatelets</b>			
<b>Apixaban</b>	EFV, ETR, NVP	↓ apixaban possible	Consider alternative therapy.
<b>Betrixaban</b>	All NNRTIs	↔ betrixaban expected	No dose adjustment necessary.
<b>Clopidogrel</b>	EFV, ETR	↓ activation of clopidogrel possible	ETR may prevent metabolism of clopidogrel (inactive) to its active metabolite. Avoid coadministration, if possible.
	DOR, NVP, RPV	↔ clopidogrel expected	No dose adjustment necessary.
<b>Dabigatran</b>	All NNRTIs	↔ dabigatran expected	No dose adjustment necessary.
<b>Edoxaban</b>	All NNRTIs	↔ edoxaban expected	No dose adjustment necessary.
<b>Prasugrel</b>	All NNRTIs	↔ prasugrel expected	No dose adjustment necessary.
<b>Rivaroxaban</b>	EFV, ETR, NVP	↓ rivaroxaban possible	Consider alternative therapy.
<b>Ticagrelor</b>	EFV, ETR, NVP	↓ ticagrelor expected	Consider alternative therapy.
<b>Warfarin</b>	EFV, ETR, NVP	↑ or ↓ warfarin possible	Monitor INR and adjust warfarin dose accordingly.



**Table 19b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 2 of 10)**

Concomitant Drug Class/ Name	NNRTI <sup>a</sup>	Effect on NNRTI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Anticonvulsants</b>			
Carbamazepine, Phenobarbital, Phenytoin	EFV	<u>Carbamazepine plus EFV:</u> <ul style="list-style-type: none"> <li>• Carbamazepine AUC ↓ 27%</li> <li>• EFV AUC ↓ 36%</li> </ul> <u>Phenytoin plus EFV:</u> <ul style="list-style-type: none"> <li>• ↓ EFV</li> <li>• ↓ phenytoin possible</li> </ul>	Monitor anticonvulsant and EFV concentrations or, if possible, use alternative anticonvulsant to those listed.
	ETR	↓ anticonvulsant and ETR possible	<b>Do not coadminister.</b> Consider alternative anticonvulsant.
	NVP	↓ anticonvulsant and NVP possible	Monitor anticonvulsant and NVP concentrations and virologic responses or consider alternative anticonvulsant.
	DOR, RPV	↓ <b>NNRTI</b> possible	<b>Contraindicated. Do not coadminister.</b> Consider alternative anticonvulsant.
Eslicarbazepine	All NNRTIs	↓ NNRTI possible	Monitor virologic outcomes and consider monitoring plasma concentrations of ARVs, or consider alternative anticonvulsant or ARV drug.
Oxcarbazepine	DOR, RPV	↓ <b>NNRTI</b> possible	<b>Contraindicated. Do not coadminister.</b> Consider alternative anticonvulsant.
Ethosuximide, Lacosamide, Tiagabine, Zonisamide,	ETR, EFV	↓ anticonvulsant possible	Monitor seizure control and plasma concentrations of anticonvulsants (when available).
Lamotrigine	EFV	↓ lamotrigine possible	Monitor seizure control and plasma concentrations of lamotrigine.
<b>Antidepressants</b>			
Bupropion	EFV, NVP	Bupropion AUC ↓ 55% ↓ bupropion possible	Titrate bupropion dose based on clinical response.
Citalopram, Escitalopram	EFV, ETR, NVP	↓ antidepressant possible	Titrate antidepressant dose based on clinical response.
Fluoxetine, Fluvoxamine	All NNRTIs	↔ antidepressant expected	No dose adjustment necessary.
Paroxetine	EFV, ETR	↔ paroxetine observed with EFV or ETR	No dose adjustment necessary.
	DOR, NVP, RPV	↔ expected with <b>DOR</b> , NVP or RPV	No dose adjustment necessary.
Nefazodone	EFV, ETR, NVP	↓ nefazodone expected ↑ NNRTI possible	Monitor the antidepressant effect and titrate dose as necessary. Monitor for ARV-related adverse events.
	DOR, RPV	↑ <b>NNRTI</b> possible	Monitor for ARV-related adverse events.
Sertraline	EFV	Sertraline AUC ↓ 39%	Titrate sertraline dose based on clinical response.
Trazodone	EFV, ETR, NVP	↓ trazodone possible	Monitor the therapeutic effect of trazodone and titrate dose as necessary.

**Table 19b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 3 of 10)**

Concomitant Drug Class/ Name	NNRTI <sup>a</sup>	Effect on NNRTI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Antifungals</b>			
<b>Fluconazole</b>	EFV	↔ fluconazole or EFV	No dose adjustment necessary.
	ETR	ETR AUC ↑ 86%	No dose adjustment necessary. Use with caution.
	NVP	NVP AUC ↑ 110%	Increased risk of hepatotoxicity possible with this combination. Monitor NVP toxicity or use alternative ARV agent.
	<b>DOR</b> , RPV	↑ <b>NNRTI</b> possible	No dose adjustment necessary.
<b>Isavuconazole</b>	EFV, ETR, NVP	↓ isavuconazole possible	Dose adjustments for isavuconazole may be necessary. Consider monitoring isavuconazole concentration and antifungal response.
	<b>DOR</b> , RPV	↑ <b>NNRTI</b> possible	No dose adjustment necessary.
<b>Itraconazole</b>	EFV	Itraconazole and OH-itraconazole AUC, C <sub>max</sub> and C <sub>min</sub> ↓ 35% to 44%	Failure to achieve therapeutic itraconazole concentrations has been reported. Avoid this combination if possible. If coadministered, closely monitor itraconazole concentration and adjust dose accordingly.
	ETR	↓ itraconazole possible ↑ ETR possible	Dose adjustments for itraconazole may be necessary. Monitor itraconazole level and antifungal response.
	NVP	Itraconazole AUC ↓ 61% ↑ NVP possible	Avoid this combination if possible. If coadministered, monitor itraconazole concentration and adjust dose accordingly.
	<b>DOR</b> , RPV	↑ <b>NNRTI</b> possible	No dose adjustment necessary.
<b>Posaconazole</b>	EFV	Posaconazole AUC ↓ 50% ↔ EFV	Avoid concomitant use unless the benefit outweighs the risk. If coadministered, monitor posaconazole concentration and adjust dose accordingly.
	<b>DOR</b> , ETR, NVP, RPV	↑ NNRTI possible	Monitor for NNRTI toxicities.
<b>Voriconazole</b>	EFV	Voriconazole AUC ↓ 77% EFV AUC ↑ 44%	<b>Contraindicated at standard doses.</b> <u>Dose Adjustment:</u> • Voriconazole 400 mg BID, EFV 300 mg daily
	ETR	↔ Voriconazole AUC ETR AUC ↑ 36%	No dose adjustment necessary.
	NVP	↓ voriconazole possible ↑ NVP possible	Monitor for toxicity and antifungal response and/or voriconazole concentration.
	<b>DOR</b> , RPV	↑ <b>NNRTI</b> possible	No dose adjustment necessary.
<b>Antihyperglycemics</b>			
<b>Canagliflozin, Dapagliflozin, Empagliflozin, Sitagliptin</b>	All NNRTIs	↔ antihyperglycemic expected	No dose adjustment necessary.
<b>Linagliptin, Saxagliptin</b>	EFV, ETR, NVP	↓ antihyperglycemic possible	Monitor glycemic control.

**Table 19b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 4 of 10)**

Concomitant Drug Class/ Name	NNRTI <sup>a</sup>	Effect on NNRTI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Antimalarials</b>			
<b>Artemether/ Lumefantrine</b>	EFV	Artemether AUC ↓ 79% DHA AUC ↓ 75% Lumefantrine AUC ↓ 56%	Consider alternative ARV or antimalarial drug. If used in combination, monitor closely for antimalarial efficacy.
	ETR	Artemether AUC ↓ 38% ↔ DHA AUC ↔ Lumefantrine AUC ↔ ETR AUC	Clinical significance of the reduced antimalarial drug concentrations unknown. If used in combination with ETR, monitor for antimalarial efficacy.
	NVP	Artemether AUC ↓ 67% to 72% <u>DHA:</u> • Study results are conflicting. DHA AUC ↓ 37% in one study, no difference in another. <u>Lumefantrine:</u> • Study results are conflicting. Lumefantrine AUC ↓ 25% to 58% in 2 studies but ↑ 56% in another.	Clinical significance unknown. If used, monitor closely for antimalarial efficacy and lumefantrine toxicity.
<b>Atovaquone/ Proguanil</b>	EFV	Atovaquone AUC ↓ 75% Proguanil AUC ↓ 43%	No dose recommendation. Consider alternative drug for malaria prophylaxis, if possible.
<b>Antimycobacterials</b>			
<b>Bedaquiline</b>	EFV, ETR	↓ bedaquiline possible	<b>Do not coadminister.</b>
	NVP	↔ bedaquiline AUC	No dose adjustment necessary.
<b>Clarithromycin</b>	EFV	Clarithromycin AUC ↓ 39%	Monitor for effectiveness or consider alternative agent, such as azithromycin, for MAC prophylaxis and treatment.
	ETR	Clarithromycin AUC ↓ 39% ETR AUC ↑ 42%	Consider alternative agent, such as azithromycin, for MAC prophylaxis and treatment.
	NVP	Clarithromycin AUC ↓ 31% NVP AUC ↑ 26%	Monitor for effectiveness or use alternative agent, such as azithromycin, for MAC prophylaxis and treatment.
	RPV	↔ clarithromycin expected ↑ RPV possible	Consider alternative macrolide, such as azithromycin, for MAC prophylaxis and treatment.
<b>Rifabutin</b>	<b>DOR</b>	<b>DOR AUC ↓ 50%</b>	<b>Increase DOR dose to 100 mg twice daily. No dose adjustment for rifabutin.</b>
	EFV	Rifabutin ↓ 38%	<u>Dose:</u> • Rifabutin 450–600 mg/day; or • Rifabutin 600 mg 3 times/week if EFV is not coadministered with a PI.
	ETR	↔ Rifabutin and metabolite AUC ETR AUC ↓ 37%	<b>Do not coadminister ETR plus PI/r with rifabutin.</b>  Use rifabutin 300 mg once daily if ETR is administered without PI/r

**Table 19b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 5 of 10)**

Concomitant Drug Class/ Name	NNRTI <sup>a</sup>	Effect on NNRTI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Antimycobacterials, continued</b>			
Rifabutin, continued	NVP	Rifabutin AUC ↑ 17% and metabolite AUC ↑ 24%  NVP C <sub>min</sub> ↓ 16%	No dose adjustment necessary. Use with caution.
	RPV	Rifabutin plus RPV 50 mg Once Daily Compared to RPV 25 mg Once Daily Alone: • ↔ RPV AUC and C <sub>min</sub>	Increase RPV dose to 50 mg once daily. No dose adjustment for rifabutin.
Rifampin	<b>DOR</b>	<b>DOR AUC ↓ 88%</b>	<b>Contraindicated.</b>
	EFV	EFV AUC ↓ 26%	<b>Do not use EFV 400 mg with rifampin.</b> Maintain EFV dose at 600 mg once daily and monitor for virologic response.
	ETR	Significant ↓ ETR possible	<b>Do not coadminister.</b>
	NVP	NVP ↓ 20% to 58%	<b>Do not coadminister.</b>
	RPV	RPV AUC ↓ 80%	<b>Contraindicated.</b>
Rifapentine	EFV	↔ EFV concentrations	No dose adjustment necessary.
	ETR, NVP	↓ NNRTI possible	<b>Do not coadminister.</b>
	<b>DOR</b> , RPV	↓ <b>NNRTI</b> expected	<b>Contraindicated.</b>
<b>Antipneumocystis and Antitoxoplasmosis Drugs</b>			
Atovaquone	EFV	Atovaquone AUC ↓ 44% to 47%	Consider alternative agent for PCP or toxoplasmosis treatment or use alternative ARV drug.  If used in combination, monitor therapeutic efficacy of atovaquone.
<b>Antipsychotics</b>			
<b>Aripiprazole</b>	<b>EFV, ETR, NVP</b>	↓ aripiprazole expected	Monitor effectiveness of antipsychotic. Consider doubling usual dose of aripiprazole over 1–2 weeks. Refer to aripiprazole prescribing information for dosing recommendations.
<b>Brexpiprazole</b>	<b>EFV, ETR, NVP</b>	↓ brexpiprazole expected	Monitor effectiveness of antipsychotic. Consider doubling the usual dose of brexpiprazole and making further adjustments based on clinical response. Refer to brexpiprazole prescribing information.
<b>Cariprazine</b>	<b>EFV, ETR, NVP</b>	↓ cariprazine and ↑ or ↓ active metabolite possible	Coadministration is not recommended.
Olanzapine	EFV	↓ olanzapine possible	Monitor effect of olanzapine.
	<b>DOR</b> , ETR, NVP, RPV	↔ olanzapine expected	No dose adjustment necessary.
Pimozide	EFV, <b>ETR, NVP</b>	↓ pimozide possible	Monitor therapeutic effectiveness of pimozide
Lurasidone, <b>Pimavanserin</b> , Quetiapine, Thioridazine	EFV, ETR, NVP	↓ antipsychotic possible	Monitor effect of antipsychotic.

**Table 19b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 6 of 10)**

Concomitant Drug Class/ Name	NNRTI <sup>a</sup>	Effect on NNRTI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Benzodiazepines</b>			
Alprazolam	EFV, ETR, NVP	↓ alprazolam possible	Monitor for therapeutic effectiveness of alprazolam.
Diazepam	EFV, NVP	↓ diazepam possible	Monitor for therapeutic effectiveness of diazepam.
	ETR	↑ diazepam possible	Decreased dose of diazepam may be necessary. Monitor for diazepam toxicity.
Lorazepam	EFV	↔ lorazepam AUC	No dose adjustment necessary.
	ETR, NVP	↔ lorazepam expected	
Midazolam	EFV	↑ or ↓ midazolam possible	Monitor therapeutic effectiveness and toxicity of midazolam.
	ETR	Midazolam AUC ↓ 31% Midazolam active metabolite C <sub>max</sub> ↑ 57%	Monitor therapeutic effectiveness of midazolam.
	NVP	↓ midazolam possible	Monitor therapeutic effectiveness of midazolam.
Triazolam	EFV, ETR, NVP	↓ triazolam possible	Monitor therapeutic effectiveness of triazolam.
<b>Cardiac Medications</b>			
Dihydropyridine CCBs	EFV, ETR, NVP	↓ CCBs possible	Titrate CCB dose based on clinical response.
Diltiazem, Verapamil	EFV	Diltiazem AUC ↓ 69% ↓ verapamil possible	Titrate diltiazem or verapamil dose based on clinical response.
	ETR, NVP	↓ diltiazem or verapamil possible	
<b>Corticosteroids</b>			
Dexamethasone	DOR, EFV, ETR, NVP	↓ NNRTI possible	Consider alternative corticosteroid for long-term use. If dexamethasone is used with NNRTI, monitor virologic response.
	RPV	Significant ↓ RPV possible	<b>Contraindicated with more than a single dose of dexamethasone.</b>
<b>Hepatitis C Direct-Acting Antiviral Agents</b>			
Daclatasvir	EFV, ETR, NVP	<u>Daclatasvir 120 mg Once Daily plus EFV 600 mg Daily Compared with Daclatasvir 60 mg Alone:</u> • Daclatasvir C <sub>min</sub> ↓ 17%, AUC ↑ 37%	The recommended dose is daclatasvir 90 mg once daily.
	DOR, RPV	No data	No dose adjustment necessary.
Dasabuvir plus Paritaprevir/ Ombitasivir/RTV	DOR	↑ DOR possible	No dose adjustment necessary.
	EFV	No data	<b>Contraindicated.</b>
	ETR, NVP	↓ DAAs possible	<b>Do not coadminister.</b>
	RPV	RPV AUC ↑ 150% to 225%	<b>Do not coadminister</b> , due to potential for QT interval prolongation with higher concentrations of RPV.

**Table 19b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 7 of 10)**

Concomitant Drug Class/ Name	NNRTI <sup>a</sup>	Effect on NNRTI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Hepatitis C Direct-Acting Antiviral Agents, continued</b>			
Elbasvir/ Grazoprevir	EFV	Elbasvir AUC ↓ 54% Grazoprevir AUC ↓ 83% EFV ↔ by grazoprevir EFV ↔ AUC by elbasvir	<b>Contraindicated.</b>
	ETR, NVP	↓ elbasvir and grazoprevir expected	<b>Do not coadminister.</b>
	<b>DOR</b> , RPV	↔ Elbasvir, grazoprevir ↔ DOR, RPV	No dose adjustment necessary.
Glecaprevir/ Pibrentasvir	<b>DOR</b>	<b>↑ DOR expected</b>	<b>No dose adjustment necessary.</b>
	EFV	↓ glecaprevir and pibrentasvir expected	<b>Do not coadminister.</b>
	ETR, NVP	↓ glecaprevir and pibrentasvir possible	
	RPV	↔ glecaprevir, pibrentasvir RPV AUC ↑ 84%	No dose adjustment necessary.
Ledipasvir/ Sofosbuvir	EFV	Ledipasvir AUC, C <sub>min</sub> , and C <sub>max</sub> ↓ 34% ↔ sofosbuvir	No dose adjustment necessary.
	ETR, NVP	No significant effect expected	
	<b>DOR</b> , RPV	↔ Ledipasvir, sofosbuvir ↔ DOR, RPV	
Simeprevir	<b>DOR</b>	<b>No significant effect expected.</b>	<b>No dose adjustment necessary.</b>
	EFV	Simeprevir AUC ↓ 71%, C <sub>min</sub> ↓ 91% ↔ EFV	<b>Do not coadminister.</b>
	ETR, NVP	↓ simeprevir expected	<b>Do not coadminister.</b>
	RPV	↔ simeprevir and RPV	No dose adjustment necessary.
Sofosbuvir/ Velpatasvir	EFV	Velpatasvir AUC ↓ 43%, C <sub>max</sub> ↓ 37% and C <sub>min</sub> ↓ 47%	<b>Do not coadminister.</b>
	ETR, NVP	↓ velpatasvir expected	<b>Do not coadminister.</b>
	<b>DOR</b> , RPV	No significant effect expected	No dose adjustment necessary.
Sofosbuvir/ Velpatasvir/ Voxilaprevir	EFV	Velpatasvir AUC ↓ 43%, C <sub>max</sub> ↓ 37%, and C <sub>min</sub> ↓ 47% ↓ voxilaprevir expected	<b>Do not coadminister.</b>
	ETR, NVP	↓ voxilaprevir expected ↓ velpatasvir expected	<b>Do not coadminister.</b>
	<b>DOR</b> , RPV	No significant effect expected	No dose adjustment necessary.

**Table 19b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 8 of 10)**

Concomitant Drug Class/ Name	NNRTI <sup>a</sup>	Effect on NNRTI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Herbal Products</b>			
St. John's Wort	EFV, ETR, NVP	↓ EFV, ETR, and NVP expected	<b>Do not coadminister.</b>
	DOR, RPV	↓ NNRTI expected	<b>Contraindicated.</b>
<b>Hormonal Therapies</b>			
Hormonal Contraceptives, Oral	EFV	↔ Ethinyl estradiol Etonogestrel (metabolite of oral desogestrel) C <sub>min</sub> ↓ 61% Levonorgestrel (metabolite of oral norgestimate) AUC ↓ 83% Norelgestromin (metabolite of oral norgestimate) AUC ↓ 64%	Use alternative or additional contraceptive methods.
	ETR	Ethinyl estradiol AUC ↑ 22% No significant effect on norethindrone	No dose adjustment necessary.
	NVP	Ethinyl estradiol AUC ↓ 29%, C <sub>min</sub> ↓ 58% Norethindrone AUC ↓ 18% Etonogestrel (metabolite of oral desogestrel) C <sub>min</sub> ↓ 22%	Based on clinical data demonstrating no change in effectiveness, no dose adjustment necessary.
	RPV	↔ Ethinyl estradiol ↔ Norethindrone	No dose adjustment necessary.
	<b>DOR</b>	↔ Ethinyl estradiol ↔ Levonorgestrel	<b>No dose adjustment necessary.</b>
	Depot Medroxy-progesterone Acetate (MPA) Injectable	EFV, NVP	DMPA: no significant change
Etonogestrel-Releasing Subdermal Implant	EFV	Etonogestrel AUC ↓ 63% to 82%	Use alternative or additional contraceptive methods.
	NVP	Etonogestrel: no significant change	No dose adjustment necessary.
<b>Etonogestrel/ Ethinyl Estradiol Vaginal Ring</b>	<b>EFV</b>	<b>Ethinyl estradiol (intravaginal ring) AUC ↓ 56%</b> <b>Etonogestrel (intravaginal ring) AUC ↓ 81%</b>	<b>Use alternative or additional contraceptive methods.</b>
Levonorel-Release Subdermal Implant	EFV	Levonorgestrel AUC ↓ 47%	Use alternative or additional contraceptive methods. Unintended pregnancies were observed in women who used EFV and levonorgestrel implant concomitantly.
	NVP	Levonorgestrel AUC ↑ 35%	No dose adjustment necessary.
Levonorgestrel For emergency contraception	EFV	Levonorgestrel AUC ↓ 58%	Effectiveness of emergency postcoital contraception may be diminished.

**Table 19b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 9 of 10)**

Concomitant Drug Class/ Name	NNRTI <sup>a</sup>	Effect on NNRTI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Hormonal Therapies, continued</b>			
<b>Menopausal Hormone Replacement Therapy</b>	EFV, ETR, NVP	<p>↓ estrogen possible with estradiol or conjugated estrogen (equine and synthetic)</p> <p>↓ medroxyprogesterone possible</p> <p>↓ micronized progesterone possible</p> <p>↓ drospirenone possible</p> <p>See Hormonal Contraceptives for other progestin-NNRTI interactions</p>	Monitor menopausal symptoms. Titrate to the dose of hormonal therapy that achieves menopausal symptom relief.
<b>Gender-Affirming Hormone Therapy</b>	EFV, ETR, NVP	<p>↓ estradiol possible</p> <p>↔ goserelin, leuprolide acetate, and spironolactone expected</p> <p>↓ dutasteride and finasteride possible</p>	Monitor feminizing effects of estrogen and antiandrogen therapy and titrate dosing as necessary to achieve therapeutic goals.
	EFV, ETR, NVP	↓ testosterone possible	Monitor masculinizing effects of testosterone and titrate testosterone dose as necessary to achieve therapeutic goals.
<b>HMG-CoA Reductase Inhibitors</b>			
<b>Atorvastatin</b>	EFV, ETR	Atorvastatin AUC ↓ 32% to 43%	Adjust atorvastatin dose according to lipid response, but do not exceed the maximum recommended dose.
	NVP	↓ atorvastatin possible	Adjust atorvastatin dose according to lipid response, but do not exceed the maximum recommended dose.
	<b>DOR</b> , RPV	↔ atorvastatin AUC	No dose adjustment necessary.
<b>Fluvastatin</b>	EFV, ETR	↑ fluvastatin possible	Dose adjustments for fluvastatin may be necessary. Monitor for fluvastatin toxicity.
<b>Lovastatin, Simvastatin</b>	EFV	<p>Simvastatin AUC ↓ 68%</p> <p>Simvastatin active metabolite AUC ↓ 60%</p>	Adjust simvastatin dose according to lipid response, but do not exceed the maximum recommended dose. If EFV is used with a PI/r, simvastatin and lovastatin should be avoided.
	ETR, NVP	<p>↓ lovastatin possible</p> <p>↓ simvastatin possible</p>	Adjust lovastatin or simvastatin dose according to lipid responses but do not exceed the maximum recommended dose. If ETR or NVP is used with a PI/r, simvastatin and lovastatin should be avoided.
<b>Pitavastatin</b>	EFV	↔ pitavastatin AUC	No dose adjustment necessary.
	<b>DOR</b> , ETR, NVP, RPV	↔ pitavastatin expected	No dose adjustment necessary.
<b>Pravastatin</b>	EFV	Pravastatin AUC ↓ 44%	Adjust statin dose according to lipid responses, but do not exceed the maximum recommended dose.
	ETR	↓ pravastatin possible	
<b>Rosuvastatin</b>	EFV, ETR, NVP	↔ rosuvastatin expected	No dose adjustment necessary.



**Table 19b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 10 of 10)**

Concomitant Drug Class/ Name	NNRTI <sup>a</sup>	Effect on NNRTI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Immunosuppressants</b>			
<b>Cyclosporine, Everolimus, Sirolimus, Tacrolimus</b>	EFV, ETR, NVP	↓ immunosuppressant possible	Increase in immunosuppressant dose may be necessary. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with specialist as necessary.
<b>Narcotics/Treatments for Opioid Dependence</b>			
<b>Buprenorphine</b> Sublingual or buccal	EFV	Buprenorphine AUC ↓ 50% Norbuprenorphine <sup>b</sup> AUC ↓ 71%	No dose adjustment recommended; monitor for withdrawal symptoms.
	ETR	Buprenorphine AUC ↓ 25%	No dose adjustment necessary.
	NVP	No significant effect	No dose adjustment necessary.
<b>Buprenorphine Implant</b>	EFV, ETR, NVP	No data	Clinical monitoring is recommended if NNRTI is initiated after insertion of buprenorphine implant.
<b>Methadone</b>	EFV	Methadone AUC ↓ 52%	Opioid withdrawal common; increased methadone dose often necessary.
	<b>DOR</b> , ETR	No significant effect	No dose adjustment necessary.
	NVP	Methadone AUC ↓ 37% to 51% No significant effect on NVP	Opioid withdrawal is common; increased methadone dose is often necessary.
	RPV	R-methadone <sup>c</sup> AUC ↓ 16%	No dose adjustment necessary, but monitor for withdrawal symptoms.
<b>PDE5 Inhibitors</b>			
<b>Sildenafil</b>	<b>DOR</b> , RPV	↔ sildenafil expected	<b>No dose adjustment necessary.</b>
	ETR	Sildenafil AUC ↓ 57%	May need to titrate sildenafil dose based on clinical effect.
	EFV, NVP	↓ sildenafil possible	
<b>Tadalafil</b>	EFV, ETR, NVP	↓ tadalafil possible	May need to titrate tadalafil dose based on clinical effect.
	<b>RPV</b>	↔ tadalafil	<b>No dose adjustment necessary.</b>
<b>Avanafil, Vardenafil</b>	EFV, ETR, NVP	↓ PDE5 inhibitor possible	May need to increase PDE5 inhibitor dose based on clinical effect.
<b>Miscellaneous Drugs</b>			
<b>Enzalutamide</b>	All NNRTIs	↓ NNRTI expected	<b>Contraindicated.</b>
<b>Mitotane</b>	All NNRTIs	↓ NNRTI expected	<b>Contraindicated.</b>

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

<sup>b</sup> Norbuprenorphine is an active metabolite of buprenorphine.

<sup>c</sup> R-methadone is the active form of methadone.

**Key to Symbols:**

↑ = increase

↓ = decrease

↔ = no change

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

**Table 19c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents) (Last updated October 25, 2018; last reviewed October 25, 2018)**  
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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.

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

Concomitant Drug Class/ Name	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosage Recommendations and Clinical Comments
<b>Cytomegalovirus and Hepatitis B Antivirals</b>			
<b>Adefovir</b>	TDF	No data	<b>Do not coadminister.</b> Serum concentrations of TDF and/or other renally eliminated drugs may increase.
<b>Ganciclovir, Valganciclovir</b>	<b>TAF</b> , TDF	No data	Serum concentrations of ganciclovir and/or <b>TFV</b> may increase. Monitor for dose-related toxicities.
	ZDV	No significant effect	Potential increase in hematologic toxicities.
<b>Hepatitis C Antiviral Agents</b>			
<b>Glecaprevir/Pibrentasvir</b>	TAF, TDF	No significant effect	No dose adjustment necessary.
<b>Ledipasvir/Sofosbuvir, Sofosbuvir/Velpatasvir, Sofosbuvir/Velpatasvir/ Voxilaprevir</b>	TAF	No significant effect	No dose adjustment.
	TDF	Ledipasvir ↑ TFV AUC 40% to 98% when TDF is given with RPV and EFV  Further ↑ TFV possible if TDF is given with PIs	No dose adjustment necessary.  The safety of increased TFV exposure when ledipasvir/sofosbuvir is coadministered with TDF plus a PI/r or PI/c has not been established. Consider alternative HCV or ARV drugs to avoid increased TFV toxicities.  Consider using TAF in patients at risk of TDF-associated adverse events. If TDF is used in these patients, monitor for TDF toxicity.  <b>Coadministration of ledipasvir/sofosbuvir with EVG/c/TDF/FTC is not recommended.</b>
<b>Ribavirin</b>	<b>TDF</b>	<b>With Sofosbuvir 400 mg:</b>  • ↔ TFV AUC	<b>No dose adjustment necessary.</b>
	ZDV	Ribavirin inhibits phosphorylation of ZDV.	Avoid coadministration if possible, or closely monitor HIV virologic response and possible hematologic toxicities.
<b>INSTIs</b>			
<b>DTG</b>	TAF	↔ TAF AUC	No dose adjustment necessary.
	TDF	↔ TDF AUC  ↔ DTG AUC	No dose adjustment necessary.
<b>RAL</b>	TDF	RAL AUC ↑ 49%	No dose adjustment necessary.
<b>Narcotics/Treatment for Opioid Dependence</b>			
<b>Buprenorphine</b>	3TC, TDF, TAF, ZDV	No significant effect	No dose adjustment necessary.

**Table 19c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents) (Last updated October 25, 2018; last reviewed October 25, 2018)**  
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Concomitant Drug Class/ Name	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosage Recommendations and Clinical Comments
<b>Narcotics/Treatment for Opioid Dependence, continued</b>			
Methadone	ABC	Methadone clearance ↑ 22%	No dose adjustment necessary.
	ZDV	ZDV AUC ↑ 29% to 43%	Monitor for ZDV-related adverse effects.
<b>Other</b>			
Atovaquone	ZDV	ZDV AUC ↑ 31%	Monitor for ZDV-related adverse effects.
<b>Anticonvulsants</b> Carbamazepine, oxcarbazepine, phenobarbital, phenytoin	TAF	With Carbamazepine: • TAF AUC ↓ 55%  ↓ TAF possible with other anticonvulsants	<b>Coadministration is not recommended.</b>
<b>Antimycobacterial</b> Rifampin	TAF	TAF AUC ↓ 55%  TFV-DP (intracellular active moiety) AUC ↓ 36%  TAF plus Rifampin Compared with TDF Alone: • TFV-DP (intracellular active moiety) AUC ↑ 4.2-fold  With Twice-Daily TAF 25 mg Compared with Once-Daily TAF without Rifampin: • TAF AUC ↓ 14% • TFV-DP (intracellular active moiety) AUC ↓ 24%	<b>Coadministration is not recommended.</b>
	TDF	↔ AUC TFV	No dose adjustment necessary.
Rifabutin, Rifapentine	TAF	↓ TAF possible	<b>Coadministration is not recommended.</b>
St. John's Wort	TAF	↓ TAF possible	<b>Coadministration is not recommended.</b>
<b>PIs (HIV)</b>			
ATV (Unboosted), ATV/c, ATV/r	TAF	TAF 10 mg with ATV/r: • TAF AUC ↑ 91%  TAF 10 mg with ATV/c: • TAF AUC ↑ 75%	No dose adjustment (use TAF 25 mg).
	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%	<b>Avoid concomitant use without RTV or COBI.</b>  Dose: • ATV 300 mg daily plus (RTV 100 mg or COBI 150 mg) daily when coadministered with TDF 300 mg daily  • If using TDF and 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 toxicity.
	ZDV	With ATV (Unboosted): • ZDV C <sub>min</sub> ↓ 30% and ↔ ZDV AUC	Clinical significance unknown.

**Table 19c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents) (Last updated October 25, 2018; last reviewed October 25, 2018)**  
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Concomitant Drug Class/ Name	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosage Recommendations and Clinical Comments
<b>PIs (HIV), continued</b>			
<b>DRV/c</b>	TAF	<u>TAF 25 mg with DRV/c:</u> • ↔ TAF	No dose adjustment necessary.
	TDF	↑ TDF possible	Monitor for TDF-associated toxicity.
<b>DRV/r</b>	TAF	<u>TAF 10 mg with DRV/r:</u> • ↔ TAF	No dose adjustment necessary.
	TDF	TFV AUC ↑ 22% and C <sub>min</sub> ↑ 37%	Clinical significance unknown. Monitor for TDF-associated toxicity.
<b>LPV/r</b>	TAF	<u>TAF 10 mg with DRV/r:</u> • TAF AUC ↑ 47%	No dose adjustment necessary.
	TDF	↔ LPV/r AUC TFV AUC ↑ 32%	Clinical significance unknown. Monitor for TDF-associated toxicity.
<b>TPV/r</b>	ABC	ABC AUC ↓ 35% to 44%	Appropriate doses for this combination have not been established.
	TAF	↓ TAF expected	<b>Coadministration is not recommended.</b>
	TDF	↔ TDF AUC TPV AUC ↓ 9% to 18% and C <sub>min</sub> ↓ 12% to 21%	No dose adjustment necessary.
	ZDV	ZDV AUC ↓ 31% to 42% ↔ TPV AUC	Appropriate doses for this combination have not been established.

**Key to Symbols:**

↑ = increase

↓ = decrease

↔ = no change

**Key to Acronyms:** 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 = elvitegravir; FDA = Food and Drug Administration; FTC = emtricitabine; HCV = hepatitis C virus; INSTI = integrase strand transfer inhibitors; LPV/r = lopinavir/ritonavir; 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

**Table 19d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 1 of 15)

This table provides information on known or predicted PK interactions between INSTIs (BIC, DTG, EVG, or RAL) and non-ARV drugs. EVG is always coadministered with COBI. Recommendations for managing a particular drug interaction may differ depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or 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.

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia</b>			
Alfuzosin	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ alfuzosin expected	<b>Contraindicated.</b>
Doxazosin	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ doxazosin possible	Initiate doxazosin at lowest dose and titrate while monitoring for clinical response/toxicity. Dose reduction may be necessary.
Tamsulosin	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ tamsulosin expected	<b>Coadministration is not recommended.</b> If coadministered, monitor for tamsulosin toxicities.
Terazosin	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ terazosin possible	Initiate terazosin at lowest dose and titrate while monitoring for clinical response/toxicity. Dose reduction may be necessary.
Silodosin	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ silodosin expected	<b>Contraindicated.</b>
<b>Acid Reducers</b>			
Al, Mg, +/- Ca-Containing Antacids  Please refer to the Miscellaneous Drugs section of this table for recommendations on use with other polyvalent cation products (e.g., Fe, Ca supplements, multivitamins).	BIC	↔ BIC AUC if antacid is given 2 hours after BIC and under fasting conditions  BIC AUC ↓ 79% if given simultaneously with antacid  BIC AUC ↓ 52% if antacid is given 2 hours before BIC	<b>With Antacids Containing Al/Mg or Ca:</b>  • BIC can be taken under fasting conditions at least 2 hours before antacids containing Al/Mg or Ca.  Do not coadminister BIC simultaneously with, or 2 hours after, antacids containing Al/Mg or Ca.
	DTG	DTG AUC ↓ 74% if given simultaneously with antacid  DTG AUC ↓ 26% if given 2 hours before antacid	Give DTG at least 2 hours before or at least 6 hours after antacids containing polyvalent cations.
	EVG/c	EVG AUC ↓ 40% to 50% if given simultaneously with antacid  EVG AUC ↓ 15% to 20% if given 2 hours before or after antacid; ↔ with 4-hour interval	Separate EVG/c/TDF/FTC and antacid administration by >2 hours.

**Table 19d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 2 of 15)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Acid Reducers, continued</b>			
Al, Mg, +/- <b>Ca-Containing Antacids, continued</b> Please refer to the Miscellaneous Drugs section of this table for recommendations on use with other polyvalent cation products (e.g., Fe, Ca supplements, multivitamins).	RAL	<u>Al/Mg Hydroxide Antacid:</u> • RAL C <sub>min</sub> ↓ 49% to 63%  <u>CaCO<sub>3</sub> Antacid:</u> • RAL (400 mg BID) C <sub>min</sub> ↓ 32% • RAL (1200 mg once daily) C <sub>min</sub> ↓ 48% to 57%	<b>Do not coadminister RAL and Al-Mg hydroxide antacids.</b> Use alternative acid reducing agent.  <u>With CaCO<sub>3</sub> Antacids:</u> • RAL 1200 mg once daily: <b>Do not coadminister.</b> • RAL 400 mg BID: No dose adjustment or separation necessary.
	<b>H2-Receptor Antagonists</b>	<b>BIC, DTG, EVG/c</b>  RAL	No significant effect  RAL AUC ↑ 44% and C <sub>max</sub> ↑ 60%
<b>PPIs</b>	<b>BIC, DTG, EVG/c</b>	No significant effect	No dose adjustment necessary.
	RAL	RAL AUC ↑ 37% and C <sub>min</sub> ↑ 24%	No dose adjustment necessary.
<b>Anticoagulants and Antiplatelets</b>			
<b>Apixaban</b>	<b>BIC, DTG, RAL</b>	↔ expected	No dose adjustment necessary.
	EVG/c	↑ apixaban expected	<u>In Patients Requiring Apixaban 2.5 mg Twice Daily:</u> • <b>Coadministration is not recommended.</b>  <u>In Patients Requiring Apixaban 5 mg or 10 mg Twice Daily:</u> • Reduce apixaban dose by 50%.
<b>Betrixaban</b>	<b>BIC, DTG, RAL</b>	↔ expected	No dose adjustment necessary.
	EVG/c	↑ betrixaban expected	Administer initial single dose of betrixaban 80 mg, followed by betrixaban 40 mg once daily.
<b>Dabigatran</b>	<b>BIC, DTG, RAL</b>	↔ expected	No dose adjustment necessary.
	EVG/c	↑ dabigatran expected  Dabigatran AUC ↑ 110% to 127% with COBI 150 mg alone	Dabigatran dosing recommendation depends on indication and renal function. Refer to dabigatran prescribing information for dosing instruction when used with P-gp inhibitors.
<b>Edoxaban</b>	<b>BIC, DTG, RAL</b>	↔ expected	No dose adjustment necessary.
	EVG/c	↔ or ↑ edoxaban expected	<u>For Stroke Prevention in Nonvalvular Atrial Fibrillation:</u> • No dose adjustment necessary.  <u>For Deep Venous Thrombosis and Pulmonary Embolism:</u> • Administer edoxaban 30 mg once daily.
<b>Rivaroxaban</b>	<b>BIC, DTG, RAL</b>	↔ expected	No dose adjustment necessary.
	EVG/c	↑ rivaroxaban expected	<b>Coadministration is not recommended.</b>

**Table 19d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 3 of 15)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Anticoagulants and Antiplatelets, continued</b>			
Ticagrelor	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ ticagrelor expected	Coadministration is not recommended.
Vorapaxar	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ vorapaxar expected	Coadministration is not recommended.
Warfarin	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ or ↓ warfarin possible	Monitor INR and adjust warfarin dose accordingly.
<b>Anticonvulsants</b>			
Carbamazepine	BIC	↓ BIC possible	Consider using an alternative anticonvulsant or ARV.
	DTG	DTG AUC ↓ 49%	Increase DTG dose to 50 mg BID in treatment-naïve or treatment-experienced, INSTI-naïve patients.  Use alternative anticonvulsant for INSTI-experienced patients with known or suspected INSTI resistance.
	EVG/c	Carbamazepine AUC ↑ 43% EVG AUC ↓ 69% and C <sub>min</sub> ↓ >99% ↓ COBI expected	<b>Contraindicated.</b>
	RAL	↓ or ↔ RAL possible	<b>Coadministration is not recommended.</b>
Eslicarbazepine	All INSTIs	↓ INSTI possible ↓ COBI possible	Consider using an alternative anticonvulsant or ARV.
Ethosuximide	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ ethosuximide possible	Clinically monitor for ethosuximide toxicities.
Lamotrigine	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	No data	Monitor anticonvulsant level and adjust dose accordingly.
Oxcarbazepine	All INSTIs	↓ INSTI possible ↓ COBI possible	Consider using an alternative anticonvulsant or ARV.
Phenobarbital Phenytoin	BIC	↓ BIC possible	<b>Coadministration is not recommended.</b>
	DTG	↓ DTG possible	<b>Coadministration is not recommended.</b>
	EVG/c	↓ EVG/c expected	<b>Contraindicated.</b>
	RAL	↓ or ↔ RAL possible	<b>Coadministration is not recommended.</b>
Valproic Acid	All INSTIs	No data	Monitor valproic acid concentration and virologic response.

**Table 19d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 4 of 15)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Antidepressants/Anxiolytics/Antipsychotics</b> Also see Sedative/Hypnotics section below.			
<b>Aripiprazole</b>	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ aripiprazole expected	Administer 25% of the usual aripiprazole dose. Titrate based on clinical monitoring for efficacy and toxicity. Refer to aripiprazole label for dosing recommendations in patients who are known to be CYP2D6 poor metabolizers or who have major depressive disorder.
<b>Brexpiprazole</b>	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ brexpiprazole expected	Administer 25% of the usual brexpiprazole dose. Titrate based on clinical monitoring for efficacy/toxicity. Refer to brexpiprazole label for dosing recommendations in patients who are known to be CYP2D6 poor metabolizers or who have major depressive disorder.
<b>Bupropion</b>	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ bupropion possible	Titrate bupropion dose based on clinical response.
<b>Buspirone</b>	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ buspirone possible	Initiate buspirone at a low dose. Dose reduction may be necessary.
<b>Cariprazine</b>	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ cariprazine expected	<p><u>Starting Cariprazine in a Patient Already on EVG/c:</u></p> <ul style="list-style-type: none"> <li>• Administer cariprazine 1.5 mg on Day 1 and Day 3, with no dose given on Day 2.</li> <li>• From Day 4 onward, administer 1.5 mg daily. Can be increased to a maximum dose of 3 mg daily.</li> <li>• If EVG/c is withdrawn, cariprazine dose may need to be increased.</li> </ul> <p><u>Starting EVG/c in a Patient Already on Cariprazine:</u></p> <ul style="list-style-type: none"> <li>• For patients receiving cariprazine 3 mg or 6 mg daily, reduce cariprazine dose by half.</li> <li>• For patients taking cariprazine 4.5 mg daily, the dose should be reduced to 1.5 mg or 3 mg daily.</li> <li>• For patients taking cariprazine 1.5 mg daily, change to 1.5 mg every other day.</li> <li>• If EVG/c is withdrawn, cariprazine dose may need to be increased.</li> </ul>



**Table 19d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 5 of 15)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Antidepressants/Anxiolytics/Antipsychotics, continued</b> Also see Sedative/Hypnotics section below.			
Fluvoxamine	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ or ↓ EVG possible	Consider alternative antidepressant or ARV.
Lurasidone	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ lurasidone expected	Contraindicated.
Pimavanserin	BIC, DTG, RAL	↔ expected	Standard doses.
	EVG/c	↑ pimavanserin expected	Reduce pimavanserin dose by 50%. Titrate dose based on efficacy and toxicity.
Pimozide	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ pimozide expected	Contraindicated.
Quetiapine	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ quetiapine AUC expected	<p><u>Initiation of Quetiapine in a Patient Receiving EVG/c:</u></p> <ul style="list-style-type: none"> <li>Start quetiapine at the lowest dose and titrate up as needed. Monitor for quetiapine efficacy and adverse effects.</li> </ul> <p><u>Initiation of EVG/c in a Patient Receiving a Stable Dose of Quetiapine:</u></p> <ul style="list-style-type: none"> <li>Reduce quetiapine dose to 1/6 of the original dose, and closely monitor for quetiapine efficacy and adverse effects.</li> </ul>
SSRIs Citalopram, escitalopram, fluoxetine, paroxetine, sertraline	EVG/c	↔ EVG ↔ sertraline ↑ other SSRI possible	No dose adjustment necessary.  Initiate with lowest dose of SSRI and titrate dose carefully based on antidepressant response.
	BIC, DTG, RAL	↔ BIC, DTG, RAL expected ↔ SSRI expected	No dose adjustment necessary.
TCAs Amitriptyline, desipramine, doxepin, imipramine, nortriptyline	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	Desipramine AUC ↑ 65% ↑ TCA expected	Initiate with lowest dose of TCA and titrate dose carefully. Initiate with lowest dose of TCA and titrate dose carefully based on antidepressant response and/or drug levels.
Trazodone	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ trazodone possible	Initiate with lowest dose of trazodone and titrate dose carefully.
Other Antipsychotics (CYP3A4 and/or CYP2D6 substrates)	EVG/c	↑ antipsychotic possible	Initiate antipsychotic at a low dose. Decrease in antipsychotic dose may be necessary.

**Table 19d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 6 of 15)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Antifungals</b>			
Isavuconazole	BIC	↑ BIC possible	No dose adjustment necessary.
	EVG/c	↑ isavuconazole expected ↑ EVG and COBI possible	If coadministered, consider monitoring isavuconazole concentrations and assess virologic response.
Itraconazole	BIC	↑ BIC expected	No dose adjustment necessary.
	DTG, RAL	↔ expected	No dose adjustment necessary.
EVG/c		↑ itraconazole expected ↑ EVG and COBI possible	Consider monitoring itraconazole level to guide dosage adjustments. High itraconazole doses (>200 mg/day) are not recommended unless dose is guided by itraconazole levels.
	Posaconazole	BIC	↑ BIC expected
EVG/c	DTG, RAL	↔ expected	No dose adjustment necessary.
		↑ EVG and COBI possible ↑ posaconazole possible	If coadministered, monitor posaconazole concentrations.
Voriconazole	BIC	↑ BIC possible	No dose adjustment necessary.
	DTG, RAL	↔ expected	No dose adjustment necessary.
EVG/c		↑ voriconazole expected ↑ EVG and COBI possible	<b>Do not coadminister voriconazole and COBI unless benefit outweighs risk.</b> If coadministered, consider monitoring voriconazole concentrations and adjust dose accordingly.
	<b>Antihyperglycemics</b>		
Metformin	BIC	Metformin AUC ↑ 39%	Monitor for metformin adverse effects.
	DTG	DTG 50 mg Once Daily plus Metformin 500 mg BID: • Metformin AUC ↑ 79% and C <sub>max</sub> ↑ 66%	Start metformin at lowest dose and titrate based on glycemic control. Monitor for metformin adverse effects.  When starting/stopping DTG in patients on metformin, dose adjustment of metformin may be necessary to maintain optimal glycemic control and/or minimize adverse effects of metformin.
		DTG 50 mg BID plus Metformin 500 mg BID: • Metformin AUC ↑ 2.4-fold and C <sub>max</sub> ↑ 2-fold	
RAL	↔ expected	No dose adjustment necessary.	
Saxagliptin	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ saxagliptin expected	Limit saxagliptin dose to 2.5 mg once daily.
Dapagliflozin/ Saxagliptin	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ saxagliptin expected	<b>Do not coadminister</b> , as this coformulated drug contains 5 mg of saxagliptin.
<b>Antimycobacterials</b>			
Clarithromycin	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ clarithromycin possible ↑ COBI possible	CrCl 50–60 mL/min: • Reduce clarithromycin dose by 50%  CrCl <50 mL/min: • EVG/c is not recommended.

**Table 19d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 7 of 15)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Antimycobacterials, continued</b>			
Rifabutin	<b>BIC</b>	<b>Rifabutin (300 mg Once Daily):</b> • BIC AUC ↓ 38% and C <sub>min</sub> ↓ 56%	<b>Do not coadminister.</b>
	DTG	Rifabutin (300 mg Once Daily): • DTG AUC ↔ and C <sub>min</sub> ↓ 30%	No dose adjustment necessary.
	EVG/c	Rifabutin 150 mg Every Other Day with EVG/c Once Daily Compared to Rifabutin 300 mg Once Daily Alone: • ↔ rifabutin AUC • 25-O-desacetyl-rifabutin AUC ↑ 625% • EVG AUC ↓ 21% and C <sub>min</sub> ↓ 67%	<b>Do not coadminister.</b>
	RAL	RAL AUC ↑ 19% and C <sub>min</sub> ↓ 20%	No dose adjustment necessary.
Rifampin	<b>BIC</b>	<b>BIC AUC ↓ 75%</b>	<b>Contraindicated.</b>
	DTG	Rifampin with DTG 50 mg BID Compared to DTG 50 mg BID Alone: • DTG AUC ↓ 54% and C <sub>min</sub> ↓ 72%  Rifampin with DTG 50 mg BID Compared to DTG 50 mg Once Daily Alone: • DTG AUC ↑ 33% and C <sub>min</sub> ↑ 22%	<b>Dose:</b> • DTG 50 mg BID (instead of 50 mg once daily) for patients without suspected or documented INSTI mutation.  Alternative to rifampin should be used in patients with certain suspected or documented INSTI-associated resistance substitutions. Consider using rifabutin.
	EVG/c	Significant ↓ EVG and COBI expected	<b>Contraindicated.</b>
Rifampin	RAL	RAL 400 mg: • RAL AUC ↓ 40% and C <sub>min</sub> ↓ 61%  Rifampin with RAL 800 mg BID Compared to RAL 400 mg BID Alone: • RAL AUC ↑ 27% and C <sub>min</sub> ↓ 53%	<b>Dose:</b> • RAL 800 mg BID, instead of 400 mg BID  <b>Do not coadminister RAL 1200 mg once daily with rifampin.</b>  Monitor closely for virologic response or consider using rifabutin as an alternative rifamycin.
	Rifapentine	<b>BIC, DTG, EVG/c</b>	Significant ↓ <b>BIC, DTG, EVG, and COBI</b> expected
Rifapentine	RAL	Rifapentine 900 mg Once Weekly: • RAL AUC ↑ 71% and C <sub>min</sub> ↓ 12%  Rifapentine 600 mg Once Daily: • RAL C <sub>min</sub> ↓ 41%	For once-weekly rifapentine, use standard RAL 400 mg BID doses.  <b>Do not coadminister with once-daily rifapentine.</b>

**Table 19d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 8 of 15)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Cardiac Medications</b>			
<b>Antiarrhythmics</b> Amiodarone, bepridil, digoxin, disopyramide, dronedarone, flecainide, systemic lidocaine, mexilitine, propafenone, quinidine	BIC, DTG	↔ expected for the listed antiarrhythmics, except for disopyramide ↑ disopyramide possible	No dose adjustment necessary. Coadminister with caution. Clinical monitoring is recommended.
	RAL	↔ expected for the listed antiarrhythmics	No dose adjustment necessary.
	EVG/c	↑ antiarrhythmics possible Digoxin C <sub>max</sub> ↑ 41% and no significant change in AUC	Use antiarrhythmics with caution. TDM, if available, is recommended for antiarrhythmics.
<b>Bosentan</b>	BIC, DTG	↓ BIC, DTG possible	Standard doses.
	RAL	↔ expected	No dose adjustment necessary.
	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.
<b>Beta-blockers</b> (e.g., metoprolol, timolol)	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ beta-blockers possible	Beta-blocker dose may need to be decreased; adjust dose based on clinical response.  Consider using beta-blockers that are not metabolized by CYP450 enzymes (e.g., atenolol, labetalol, nadolol, sotalol).
<b>CCBs</b>	BIC	↑ BIC possible with diltiazem ↔ expected for all other CCBs	No dose adjustment necessary.
	DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ CCBs possible	Coadminister with caution. Titrate CCB dose and monitor for CCB efficacy and toxicities.  Refer to <a href="#">Table 19a</a> for diltiazem plus ATV/r recommendations.
<b>Dofetilide</b>	BIC, DTG	↑ dofetilide expected	Contraindicated.
	RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ dofetilide possible	Do not coadminister.
<b>Eplerenone</b>	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ eplerenone expected	Contraindicated.
<b>Ranolazine</b>	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ ranolazine expected	Contraindicated.
<b>Ivabradine</b>	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ ivabradine expected	Contraindicated.

**Table 19d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 9 of 15)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Corticosteroids</b>			
<b>Beclomethasone</b> Inhaled or intranasal	<b>BIC, DTG, EVG/c, RAL</b>	↔ expected	No dose adjustment necessary.
<b>Budesonide, Ciclesonide, Fluticasone, Mometasone</b> Inhaled or intranasal	<b>BIC, DTG, RAL</b> EVG/c	↔ expected ↑ glucocorticoid possible	<b>No dose adjustment necessary.</b> Coadministration can result in adrenal insufficiency and Cushing's syndrome. <b>Do not coadminister unless potential benefits of inhaled or intranasal corticosteroid outweigh the risks of systemic corticosteroid adverse effects.</b> Consider an alternative corticosteroid (e.g., beclomethasone).
<b>Betamethasone, Budesonide</b> Systemic	<b>BIC, DTG, RAL</b> EVG/c	↔ expected ↑ glucocorticoids possible ↓ EVG possible	<b>No dose adjustment necessary.</b> Coadministration can result in adrenal insufficiency and Cushing's syndrome. <b>Do not coadminister unless potential benefits of systemic budesonide outweigh the risks of systemic corticosteroid adverse effects.</b>
<b>Dexamethasone</b> Systemic	<b>BIC</b>	↓ BIC possible	<b>Consider an alternative corticosteroid for long-term use or an alternative ARV. If coadministration is necessary, monitor virologic response to ART.</b>
	<b>DTG, RAL</b> EVG/c	↔ expected ↓ EVG and COBI possible	<b>No dose adjustment necessary.</b> Consider an alternative corticosteroid for long-term use or alternative ART. If coadministration is necessary, monitor virologic response to ART.
<b>Prednisone, Prednisolone</b> Systemic	<b>BIC, DTG, RAL</b> EVG/c	↔ expected ↑ prednisolone possible	<b>No dose adjustment necessary.</b> Coadministration may be considered if the potential benefits outweigh the risks of systemic corticosteroid adverse effects. If coadministered, monitor for adrenal insufficiency and Cushing's syndrome.
<b>Betamethasone, Methylprednisolone, Prednisolone, Triamcinolone</b> Local injections, including intra-articular, epidural, or intra-orbital	<b>BIC, DTG, RAL</b> EVG/c	↔ expected ↑ glucocorticoids expected	<b>No dose adjustment necessary.</b> <b>Do not coadminister.</b> Coadministration may result in adrenal insufficiency and Cushing's syndrome.
<b>Hepatitis C Direct Acting Antivirals</b>			
<b>Daclatasvir</b>	DTG	↔ daclatasvir	No dose adjustment necessary.
	EVG/c	↑ daclatasvir	Decrease daclastavir dose to 30 mg once daily.
	<b>BIC, RAL</b>	No data	No dose adjustment necessary.
<b>Dasabuvir plus Ombitasvir/ Paritaprevir/RTV</b>	<b>BIC, DTG</b>	No data	No dose adjustment necessary.
	EVG/c	No data	<b>Do not coadminister.</b>
	RAL	RAL AUC ↑ 134%	No dose adjustment necessary.

**Table 19d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 10 of 15)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Hepatitis C Direct Acting Antivirals, continued</b>			
Elbasvir/Grazoprevir	<b>BIC</b>	↔ <b>BIC expected</b>	<b>No dose adjustment necessary.</b>
	DTG	↔ elbasvir ↔ grazoprevir ↔ DTG	No dose adjustment necessary.
	EVG/c	↑ elbasvir and ↑ grazoprevir expected	<b>Coadministration is not recommended.</b>
	RAL	↔ elbasvir ↔ grazoprevir ↔ RAL with elbasvir RAL AUC ↑ 43% with grazoprevir	No dose adjustment necessary.
Glecaprevir/ Pibrentasvir	<b>BIC</b>	↔ <b>BIC expected</b>	<b>No dose adjustment necessary.</b>
	DTG, RAL	No significant effect	No dose adjustment necessary.
	EVG/c	Glecaprevir AUC ↑ 3-fold Pibrentasvir AUC ↑ 57% EVG AUC ↑ 47%	No dose adjustment necessary.
Ledipasvir/ Sofosbuvir	EVG/c/TDF/ FTC	↑ TDF and ↑ ledipasvir expected	<b>Do not coadminister.</b>
	EVG/c/TAF/ FTC	↔ EVG/c/TAF/FTC expected	No dose adjustment necessary.
	<b>BIC</b> , DTG, RAL	↔ DTG or RAL	No dose adjustment necessary.
Simeprevir	<b>BIC</b> , DTG, <b>RAL</b>	↔ expected	No dose adjustment necessary.
	EVG/c	↑ simeprevir expected	<b>Coadministration is not recommended.</b>
Sofosbuvir	All INSTIs	↔ expected	No dose adjustment necessary.
Sofosbuvir/ Velpatasvir	All INSTIs	↔ expected	No dose adjustment necessary.
Sofosbuvir/ Velpatasvir/ Voxilaprevir	EVG/c	<u>When Given with Sofosbuvir/Velpatasvir/ Voxilaprevir (400 mg/100 mg/100 mg) plus Voxilaprevir 100 mg:</u> • Sofosbuvir AUC ↑ 22% • ↔ velpatasvir • Voxilaprevir AUC ↑ 2-fold	No dose adjustment necessary.
	<b>BIC</b> , DTG, RAL	↔ expected	No dose adjustment necessary.
<b>Herbal Products</b>			
St. John's Wort	<b>BIC</b> , DTG	↓ <b>BIC and</b> DTG possible	<b>Do not coadminister.</b>
	EVG/c	↓ EVG and COBI possible	<b>Contraindicated.</b>

**Table 19d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 11 of 15)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Hormonal Therapies</b>			
<b>Hormonal Contraceptives</b> <b>Oral</b>	BIC, DTG, RAL	↔ ethinyl estradiol, norgestimate, and DTG or RAL	No dose adjustment necessary.
	EVG/c	Norgestimate AUC, C <sub>max</sub> and C <sub>min</sub> ↑ >2-fold Ethinyl estradiol AUC ↓ 25% and C <sub>min</sub> ↓ 44%	The effects of increases in progestin (norgestimate) are not fully known and can include insulin resistance, dyslipidemia, acne, and venous thrombosis. Weigh the risks and benefits of the drug and consider using an alternative contraceptive method.
		↑ drospirenone possible	Clinical monitoring is recommended, due to the potential for hyperkalemia.
<b>Hormonal Contraceptives</b> <b>Non-oral</b>	All INSTIs	No data	No drug-drug interaction studies have been conducted with INSTIs and non-oral routes of hormone administration. It is unclear if oral drug-drug interaction data can be extrapolated beyond oral routes of administration.
<b>Menopausal Hormone Replacement Therapy</b>	BIC, DTG, RAL	With Estradiol or Conjugated Estrogen (Equine and Synthetic): • ↔ estrogen expected ↔ drospirenone, medroxyprogesterone, or micronized progesterone expected	No dose adjustment necessary.
	EVG/c	↓ estrogen expected ↑ drospirenone possible ↑ oral medroxyprogesterone possible ↑ oral micronized progesterone possible	Adjust estrogen and progestin dose as needed based on clinical effects.
<b>Gender-Affirming Hormone Therapy</b>	BIC, DTG, RAL	↔ estrogen expected	No dose adjustment necessary.
	BIC, DTG, EVG/c, RAL	↔ finasteride, goserelin, leuprolide acetate, spironolactone expected	
	EVG/c	↓ estradiol expected ↑ dutasteride possible	Adjust dutasteride dosage as needed based on clinical effects and endogenous hormone concentrations.
	EVG/c	↑ testosterone possible	Monitor masculinizing effects of testosterone and for adverse effects and adjust testosterone dose as necessary.
	BIC, DTG, RAL	↔ testosterone expected	No dose adjustment necessary.
<b>HMG-CoA Reductase Inhibitors</b>			
<b>Atorvastatin</b>	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	Atorvastatin AUC ↑ 2.6-fold and C <sub>max</sub> ↑ 2.3-fold	Titrate statin dose carefully and use the lowest dose necessary while monitoring for toxicities. Do not exceed 20 mg atorvastatin daily.
<b>Lovastatin</b>	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	Significant ↑ lovastatin expected	Contraindicated.
<b>Pitavastatin, Pravastatin</b>	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	No data	No dose recommendation.

**Table 19d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 12 of 15)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>HMG-CoA Reductase Inhibitors, continued</b>			
Rosuvastatin	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	Rosuvastatin AUC ↑ 38% and C <sub>max</sub> ↑ 89%	Titrate statin dose carefully and use the lowest dose necessary while monitoring for toxicities.
Simvastatin	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	Significant ↑ simvastatin expected	<b>Contraindicated.</b>
<b>Immunosuppressants</b>			
Cyclosporine, Everolimus, Sirolimus, Tacrolimus	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ immunosuppressant possible	Initiate with an adjusted immunosuppressant dose to account for potential increased concentration and monitor for toxicities. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with a specialist as necessary.
<b>Narcotics/Treatment for Opioid Dependence</b>			
Buprenorphine Sublingual, buccal, or implant	BIC, DTG	↔ expected	No dose adjustment necessary.
	EVG/c	Buprenorphine AUC ↑ 35% and C <sub>min</sub> ↑ 66% Norbuprenorphine AUC ↑ 42% and C <sub>min</sub> ↑ 57%	No dose adjustment necessary. Clinical monitoring is recommended. When transferring buprenorphine from transmucosal administration to implantation, monitor to ensure buprenorphine effect is adequate and not excessive.
	RAL	↔ observed (sublingual) ↔ expected (implant)	No dose adjustment necessary.
Methadone	All INSTIs	No significant effect	No dose adjustment necessary.
<b>PDE5 Inhibitors</b>			
Avanafil	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	No data	<b>Coadministration is not recommended.</b>
Sildenafil	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ sildenafil expected	For Treatment of Erectile Dysfunction: • Start with sildenafil 25 mg every 48 hours and monitor for adverse effects of sildenafil.  For treatment of PAH: • <b>Contraindicated.</b>



**Table 19d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 13 of 15)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>PDE5 Inhibitors, continued</b>			
Tadalafil	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ tadalafil expected	<p>For Treatment of Erectile Dysfunction:</p> <ul style="list-style-type: none"> <li>Start with tadalafil 5-mg dose and do not exceed a single dose of tadalafil 10 mg every 72 hours. Monitor for adverse effects of tadalafil.</li> </ul> <p>For Treatment of PAH</p> <p><i>In Patients on EVG/c &gt;7 Days:</i></p> <ul style="list-style-type: none"> <li>Start with tadalafil 20 mg once daily and increase to tadalafil 40 mg once daily based on tolerability.</li> </ul> <p><i>In Patients on Tadalafil who Require EVG/c:</i></p> <ul style="list-style-type: none"> <li>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.</li> </ul>
Vardenafil	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ vardenafil expected	Start with vardenafil 2.5 mg every 72 hours and monitor for adverse effects of vardenafil.
<b>Sedative/Hypnotics</b>			
Clonazepam, Clorazepate, Diazepam, Estazolam, Flurazepam	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ benzodiazepines possible	<p>Dose reduction of benzodiazepine may be necessary. Initiate with low dose and clinically monitor.</p> <p>Consider alternative benzodiazepines to diazepam, such as lorazepam, oxazepam, or temazepam.</p>
Midazolam, Triazolam	BIC, RAL	↔ expected	No dose adjustment necessary.
	DTG	<p>With DTG 25 mg:</p> <ul style="list-style-type: none"> <li>↔ Midazolam AUC</li> </ul>	No dose adjustment necessary.
Suvorexant	EVG/c	↑ suvorexant expected	<b>Coadministration is not recommended.</b>
	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
Zolpidem	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ zolpidem expected	Initiate zolpidem at a low dose. Dose reduction may be necessary.

**Table 19d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 14 of 15)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Miscellaneous Drugs</b>			
Calcifediol	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ calcifediol possible	Dose adjustment of calcifediol may be required, and serum 25-hydroxyvitamin D, intact PTH, and serum Ca concentrations should be closely monitored.
Cisapride	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ cisapride expected	Contraindicated.
Colchicine	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ colchicine expected	<p><b>Do not coadminister in patients with hepatic or renal impairment.</b></p> <p>For Treatment of Gout Flares:</p> <ul style="list-style-type: none"> <li>Administer colchicine 0.6 mg for 1 dose, followed by colchicine 0.3 mg 1 hour later. Do not repeat dose for at least 3 days.</li> </ul> <p>For Prophylaxis of Gout Flares:</p> <ul style="list-style-type: none"> <li>If original dose was colchicine 0.6 mg BID, decrease to colchicine 0.3 mg once daily. If regimen was 0.6 mg once daily, decrease to 0.3 mg every other day.</li> </ul> <p>For Treatment of Familial Mediterranean Fever:</p> <ul style="list-style-type: none"> <li>Do not exceed colchicine 0.6 mg once daily or 0.3 mg BID.</li> </ul>
Enzalutamide	DTG	↓ DTG possible	Monitor for ARV efficacy.
	BIC, EVG/c	↓ BIC, EVG/c expected	Contraindicated.
	RAL	↔ expected	No dose adjustment necessary.
Ergot Derivatives	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ dihydroergotamine, ergotamine, methylergonovine expected	Contraindicated.
Dronabinol	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ dronabinol possible	Monitor for dronabinol-related adverse effects.
Eluxadoline	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ eluxadoline possible	Monitor for eluxadoline-related adverse effects.
Flibanserin	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ flibanserin expected	Contraindicated.
Mitotane	BIC, EVG/c	↓ BIC and ↓ EVG/c expected	Contraindicated.
	DTG	↓ DTG possible	Monitor for ARV efficacy.
	RAL	↔ expected	No dose adjustment necessary.

**Table 19d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 15 of 15)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Miscellaneous Drugs, continued</b>			
<b>Polyvalent Cation Supplements</b> Mg, Al, Fe, Ca, Zn, including multivitamins with minerals  <b>Note:</b> Please refer to the Acid Reducers section in this table for recommendations on use with Al-, Mg-, and Ca-containing antacids.	<b>BIC</b>	↔ BIC AUC if given simultaneously with Fe or Ca and food  BIC AUC ↓ 33% if given simultaneously with CaCO <sub>3</sub> under fasting conditions  BIC AUC ↓ 63% if given simultaneously with Fe under fasting conditions	With Supplements that Contain Ca or Fe: • BIC and supplements containing Ca or Fe can be taken together with food.  Do not coadminister BIC under fasting conditions simultaneously with, or 2 hours after, supplements containing Ca or Fe.
	<b>DTG</b>	DTG AUC ↓ 39% if given simultaneously with calcium carbonate under fasting conditions  DTG AUC ↓ 54% if given simultaneously with Fe under fasting conditions  ↔ DTG when administered with Ca or Fe supplement simultaneously with food	With Supplements That Contain Ca or Fe: • DTG and supplements containing Ca or Fe can be taken together with food; alternately, administer DTG at least 2 hours before or at least 6 hours after supplement.  Do not coadminister DTG under fasting conditions simultaneously with, or 2 hours after, supplements containing Ca or Fe.
	EVG/c, RAL	↓ INSTI possible	If coadministration is necessary, give INSTI at least 2 hours before or at least 6 hours after supplements containing polyvalent cations, including but not limited to the following products: cation-containing laxatives; Fe, Ca, or Mg supplements; and sucralfate. Monitor for virologic efficacy.  Many oral multivitamins also contain varying amounts of polyvalent cations; the extent and significance of chelation is unknown.
<b>Salmeterol</b>	<b>BIC, DTG, RAL</b>	↔ expected	No dose adjustment necessary.
	EVG/c	↑ salmeterol possible	Do not coadminister, due to potential increased risk of salmeterol-associated cardiovascular events.

**Key to Symbols:**

- ↑ = increase
- ↓ = decrease
- ↔ = no change

**Key to Acronyms:** Al = aluminum; ART = antiretroviral therapy; ARV = antiretroviral; ATV/r = atazanavir/ritonavir; AUC = area under the curve; **BIC = bicitegravir**; BID = twice daily; Ca = calcium; CaCO<sub>3</sub> = calcium carbonate; CCB = calcium channel blocker; C<sub>max</sub> = maximum plasma concentration; C<sub>min</sub> = minimum plasma concentration; COBI = cobicistat; CrCl = creatinine clearance; CYP = cytochrome P; DTG = dolutegravir; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; Fe = iron; FTC = emtricitabine; INR = international normalized ratio; INSTI = integrase strand transfer inhibitor; Mg = magnesium; PAH = pulmonary arterial hypertension; PI = protease inhibitor; PK = pharmacokinetic; PTH = parathyroid hormone; RAL = raltegravir; RTV = ritonavir; SSRI = selective serotonin reuptake inhibitors; TAF = tenofovir alafenamide; TCA = tricyclic antidepressants; TDF = tenofovir disoproxil fumarate; TDM = therapeutic drug monitoring; Zn = zinc

**Table 19e. Drug Interactions between CCR5 Antagonist (Maraviroc) and Other Drugs (Including Antiretroviral Agents) (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 1 of 3)

In the table below, “No dose adjustment necessary” 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 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.

Concomitant Drug Class/ Name	CCR5 Antagonist	Effect on CCR5 Antagonist and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Anticonvulsants</b>			
Carbamazepine, Phenobarbital, Phenytoin	MVC	↓ MVC possible	If used without a strong CYP3A inhibitor, use MVC 600 mg BID or an alternative antiepileptic agent.
<b>Antifungals</b>			
Isavuconazole	MVC	↑ MVC possible	Consider dose reduction to MVC 150 mg BID.
Itraconazole	MVC	↑ MVC possible	<u>Dose:</u> • MVC 150 mg BID
Posaconazole	MVC	↑ MVC possible	<u>Dose:</u> • MVC 150 mg BID
Voriconazole	MVC	↑ MVC possible	Consider dose reduction to MVC 150 mg BID.
<b>Antimycobacterials</b>			
Clarithromycin	MVC	↑ MVC possible	<u>Dose:</u> • MVC 150 mg BID
Rifabutin	MVC	↓ MVC possible	If used without a strong CYP3A inducer or inhibitor, no dose adjustment is necessary.  If used with a strong CYP3A inhibitor, use MVC 150 mg BID.
Rifampin	MVC	MVC AUC ↓ 64%	<u>Dose:</u> • MVC 600 mg BID  If used with a strong CYP3A inhibitor, use MVC 300 mg BID.
Rifapentine	MVC	↓ MVC expected	<b>Do not coadminister.</b>
<b>Hepatitis C Direct-Acting Antivirals</b>			
Daclatasvir	MVC	↔ MVC expected ↔ daclatasvir expected	No dose adjustment necessary.
Dasabuvir plus Ombitasvir/Paritaprevir/ RTV	MVC	↑ MVC expected	<b>Do not coadminister.</b>
<b>Elbasvir/Grazoprevir</b>	<b>MVC</b>	<b>↔ MVC expected</b>	<b>No dose adjustment necessary.</b>
Ledipasvir/Sofosbuvir	MVC	↔ MVC expected	No dose adjustment necessary.
Glecaprevir/Pibrentasvir	MVC	↔ MVC expected	No dose adjustment necessary.
Simeprevir	MVC	↔ MVC expected	No dose adjustment necessary.
Sofosbuvir	MVC	↔ MVC expected	No dose adjustment necessary.
Sofosbuvir/Velpatasvir	MVC	↔ MVC expected	No dose adjustment necessary.

**Table 19e. Drug Interactions between CCR5 Antagonist (Maraviroc) and Other Drugs (Including Antiretroviral Agents) (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 2 of 3)

Concomitant Drug Class/ Name	CCR5 Antagonist	Effect on CCR5 Antagonist and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>Hepatitis C Direct-Acting Antivirals, continued</b>			
Sofosbuvir/Velpatasvir/ Voxilaprevir	MVC	↔ MVC expected	No dose adjustment necessary.
<b>Herbal Products</b>			
St. John's Wort	MVC	↓ MVC expected	<b>Do not coadminister.</b>
<b>Hormonal Therapies</b>			
Hormonal Contraceptives	MVC	↔ Ethinyl estradiol or levonorgestrel	No dose adjustment necessary.
Menopausal Hormone Replacement Therapy	MVC	↔ MVC or hormone replacement therapies expected	No dose adjustment necessary.
Gender-Affirming Hormone Therapies	MVC	↔ MVC or gender-affirming hormones expected	No dose adjustment necessary.
<b>ARV Drugs</b>			
<b>INSTIs</b>			
<b>BIC, DTG</b>	<b>MVC</b>	<b>↔ MVC expected</b>	<b>No dose adjustment necessary.</b>
EVG/c	MVC	↑ MVC possible	<u>Dose:</u> • MVC 150 mg BID
RAL	MVC	MVC AUC ↓ 21% RAL AUC ↓ 37%	No dose adjustment necessary.
<b>NNRTIs</b>			
<b>DOR, RPV</b>	<b>MVC</b>	<b>↔ MVC expected</b>	<b>No dose adjustment necessary.</b>
EFV	MVC	MVC AUC ↓ 45%	<u>Dose:</u> • MVC 600 mg BID
ETR	MVC	MVC AUC ↓ 53%	<u>Dose:</u> • MVC 600 mg BID in the absence of a potent CYP3A inhibitor
NVP	MVC	↔ MVC AUC	<u>Without HIV PI:</u> • MVC 300 mg BID <u>With HIV PI (Except TPV/r):</u> • MVC 150 mg BID
<b>PIs</b>			
ATV with or without RTV or COBI	MVC	<u>With Unboosted ATV:</u> • MVC AUC ↑ 257% <u>With (ATV/r 300 mg/100 mg) Once Daily:</u> • MVC AUC ↑ 388%	<u>Dose:</u> • MVC 150 mg BID

**Table 19e. Drug Interactions between CCR5 Antagonist (Maraviroc) and Other Drugs (Including Antiretroviral Agents) (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 3 of 3)

Concomitant Drug Class/ Name	CCR5 Antagonist	Effect on CCR5 Antagonist and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
<b>PIs, continued</b>			
<b>DRV/c</b> or <b>DRV/r</b>	MVC	<u>With (DRV/r 600 mg/100 mg) BID:</u> • MVC AUC ↑ 305%  <u>With (DRV/r 600 mg/100 mg) BID and ETR:</u> • MVC AUC ↑ 210%	<u>Dose:</u> • MVC 150 mg BID
<b>LPV/r</b>	MVC	MVC AUC ↑ 295%  <u>With LPV/r and EFV:</u> • MVC AUC ↑ 153%	<u>Dose:</u> • MVC 150 mg BID
<b>RTV</b>	MVC	<u>With RTV 100 mg BID:</u> • MVC AUC ↑ 161%	<u>Dose:</u> • MVC 150 mg BID
<b>TPV/r</b>	MVC	<u>With (TPV/r 500 mg/200 mg) BID:</u> • ↔ MVC AUC	No dose adjustment necessary.

**Key to Symbols:**

↑ = increase

↓ = decrease

↔ = no change

**Key to Acronyms:** ARV = antiretroviral; ATV = atazanavir; ATV/r = atazanavir/ritonavir; AUC = area under the curve; **BIC = bicitegravir**; BID = twice daily; COBI = cobicistat; CYP = cytochrome P; **DOR = doravirine**; DRV = darunavir; 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 = tipranavir; TPV/r = tipranavir/ritonavir

**Table 20a. Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 1 of 2)

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

PIs		NNRTIs				
		DOR	EFV	ETR	NVP	RPV <sup>a</sup>
ATV Unboosted	PK Data	↑ DOR expected ↔ ATV expected	↔ EFV ATV AUC ↓ 74%	ETR AUC ↑ 50% and C <sub>min</sub> ↑ 58% ATV AUC ↓ 17% and C <sub>min</sub> ↓ 47%	↓ ATV possible	↑ RPV possible
	Dose	Standard doses	Do not coadminister.	Do not coadminister.	Do not coadminister.	Standard doses
ATV/c	PK Data	↑ DOR expected ↔ ATV expected	↓ ATV possible ↓ COBI possible	↓ ATV possible ↓ COBI possible	↓ ATV possible ↓ COBI possible	↑ RPV possible ↔ ATV expected
	Dose	Standard doses	EFV standard dose  <u>In ART-Naive Patients:</u> • ATV 400 mg plus COBI 150 mg once daily • <b>Do not use coformulated ATV/c 300 mg/150 mg.</b>  <u>In ART-Experienced Patients:</u> • <b>Do not coadminister.</b>	<b>Do not coadminister.</b>	<b>Do not coadminister.</b>	Standard doses
ATV/r	PK Data	↑ DOR expected ↔ ATV expected	(ATV 400 mg plus RTV 100 mg) Once Daily: • ATV concentrations similar to (ATV 300 mg plus RTV 100 mg) without EFV	(ATV 300 mg plus RTV 100 mg) Once Daily: • ETR AUC and C <sub>min</sub> both ↑ ~30% • ↔ ATV AUC and C <sub>min</sub>	(ATV 300 mg plus RTV 100 mg) Once Daily: • ATV AUC ↓ 42% and C <sub>min</sub> ↓ 72% • NVP AUC ↑ 25%	↑ RPV possible
	Dose	Standard doses	EFV standard dose  <u>In ART-Naive Patients:</u> • (ATV 400 mg plus RTV 100 mg) once daily  <u>In ART-Experienced Patients:</u> • <b>Do not coadminister.</b>	ETR standard dose  (ATV 300 mg plus RTV 100 mg) once daily	<b>Do not coadminister.</b>	Standard doses
DRV/c	PK Data	↑ DOR expected ↔ DRV expected	↓ DRV possible ↓ COBI possible	ETR 400 mg Once Daily with (DRV 800 mg plus COBI 150 mg) Once Daily: • ↔ ETR AUC and C <sub>min</sub> • ↔ DRV AUC and C <sub>min</sub> ↓ 56% • COBI AUC ↓ 30% and C <sub>min</sub> ↓ 66%	↓ DRV possible ↓ COBI possible	↔ DRV expected ↑ RPV possible
	Dose	Standard doses	Do not coadminister.	Do not coadminister.	Do not coadminister.	Standard doses

**Table 20a. Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 2 of 2)

PIs		NNRTIs				
		DOR	EFV	ETR	NVP	RPV <sup>a</sup>
DRV/r	PK Data	↑ DOR expected ↔ DRV expected	With (DRV 300 mg plus RTV 100 mg) BID: • EFV AUC ↑ 21% • ↔ DRV AUC and C <sub>min</sub> ↓ 31%	ETR 100 mg BID with (DRV 600 mg plus RTV 100 mg) BID: • ETR AUC ↓ 37% and C <sub>min</sub> ↓ 49% • ↔ DRV	With (DRV 400 mg plus RTV 100 mg) BID: • NVP AUC ↑ 27% and C <sub>min</sub> ↑ 47% • DRV AUC ↑ 24% <sup>b</sup>	RPV 150 mg Once Daily with (DRV 800 mg plus RTV 100 mg) Once Daily: • RPV AUC ↑ 130% and C <sub>min</sub> ↑ 178% • ↔ DRV
	Dose	Standard doses	Clinical significance unknown. Use standard doses and monitor patient closely. Consider monitoring drug levels.	Standard doses  Despite reduced ETR concentration, safety and efficacy of this combination have been established in a clinical trial.	Standard doses	Standard doses
LPV/r	PK Data	↑ DOR expected ↔ LPV expected	With LPV/r Tablets 500 mg/125 mg <sup>c</sup> BID: • LPV concentration similar to that of LPV/r 400 mg/100 mg BID without EFV	With LPV/r Tablets: • ETR AUC ↓ 35% (comparable to the decrease with DRV/r) • ↔ LPV AUC	With LPV/r Capsules: • LPV AUC ↓ 27% and C <sub>min</sub> ↓ 51%	RPV 150 mg Once Daily with LPV/r Capsules: • RPV AUC ↑ 52% and C <sub>min</sub> ↑ 74% • ↔ LPV
	Dose	Standard doses	LPV/r tablets 500 mg/125 mg <sup>c</sup> BID; LPV/r oral solution 533 mg/133 mg BID  EFV standard dose	Standard doses	LPV/r tablets 500 mg/125 mg <sup>c</sup> BID; LPV/r oral solution 533 mg/133 mg BID  NVP standard dose	Standard doses
TPV/r  Always use TPV with RTV	PK Data	↑ DOR expected ↔ TPV expected	With (TPV 500 mg plus RTV 100 mg) BID: • ↔ EFV • TPV AUC ↓ 31% and C <sub>min</sub> ↓ 42%  With (TPV 750 mg plus RTV 200 mg) BID: • ↔ EFV and TPV	With (TPV 500 mg plus RTV 200 mg) BID: • ETR AUC ↓ 76% and C <sub>min</sub> ↓ 82% • ↔ TPV AUC and C <sub>min</sub> ↑ 24%	With (TPV 250 mg plus RTV 200 mg) BID or with (TPV 750 mg plus RTV 100 mg) BID: • ↔ NVP • ↔ TPV expected	↑ RPV possible
	Dose	Standard doses	Standard doses	<b>Do not coadminister.</b>	Standard doses	Standard doses

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

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

<sup>c</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:**

↑ = increase

↓ = decrease

↔ = no change

**Key to Acronyms:** ART = antiretroviral therapy; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BID = twice daily; C<sub>min</sub> = minimum plasma concentration; COBI = cobicistat; **DOR = doravirine**; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; EFV = efavirenz; ETR = etravirine; LPV = lopinavir; LPV/r = lopinavir/ritonavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PK = pharmacokinetic; RPV = rilpivirine; RTV = ritonavir; TPV = tipranavir



**Table 20b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 1 of 3)

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

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
<b>NNRTIs</b>					
<b>DOR</b>	<b>PK Data</b>	↔ DOR, BIC expected	↔ DOR DTG AUC ↑ 36% and C <sub>min</sub> ↑ 27%	↑ DOR expected ↔ EVG	↔ DOR, RAL expected
	<b>Dose</b>	Standard doses	Standard doses	Standard doses	Standard doses
EFV	<b>PK Data</b>	↓ BIC expected	With DTG 50 mg Once Daily: • DTG AUC ↓ 57% and C <sub>min</sub> ↓ 75%	↑ or ↓ EVG, COBI, EFV possible	With RAL 400 mg BID: • RAL AUC ↓ 36% and C <sub>min</sub> ↓ 21%  With RAL 1200 mg Once Daily: • RAL AUC ↓ 14% and ↔ C <sub>min</sub>
	<b>Dose</b>	<b>Do not coadminister.</b>	In Patients Without INSTI Resistance: • DTG 50 mg BID  In Patients With Certain INSTI-Associated Resistance <sup>a</sup> or Clinically Suspected INSTI Resistance: • <b>Consider alternative combination.</b>	<b>Do not coadminister.</b>	Standard doses
ETR	<b>PK Data</b>	↓ BIC expected	ETR 200 mg BID plus DTG 50 mg Once Daily: • DTG AUC ↓ 71% and C <sub>min</sub> ↓ 88%  ETR 200 mg BID with (DRV 600 mg plus RTV 100 mg) BID and DTG 50 mg Once Daily: • DTG AUC ↓ 25% and C <sub>min</sub> ↓ 37%  ETR 200 mg BID with (LPV 400 mg plus RTV 100 mg) BID and DTG 50 mg Once Daily: • DTG AUC ↑ 11% and C <sub>min</sub> ↑ 28%	↑ or ↓ EVG, COBI, ETR possible	ETR 200 mg BID plus RAL 400 mg BID: • ETR C <sub>min</sub> ↑ 17% • RAL C <sub>min</sub> ↓ 34%

**Table 20b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 2 of 3)

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
NNRTIs, continued					
ETR, continued	Dose	<b>Do not coadminister.</b>	<b>Do not coadminister ETR and DTG without concurrently administering ATV/r, DRV/r, or LPV/r.</b>  <u>In Patients Without INSTI Resistance:</u> • DTG 50 mg once daily with ETR (concurrently with ATV/r, DRV/r, or LPV/r)  <u>In Patients With Certain INSTI-Associated Resistance or Clinically Suspected INSTI Resistance:</u> • DTG 50 mg BID with ETR (concurrently with ATV/r, DRV/r, or LPV/r)	<b>Do not coadminister.</b>	RAL 400 mg BID  <b>Coadministration with RAL 1200 mg once daily is not recommended.</b>
NVP	PK Data	<b>↓ BIC expected</b>	<u>With DTG 50 mg Once Daily:</u> • DTG AUC ↓ 19% and C <sub>min</sub> ↓ 34%	↑ or ↓ EVG, COBI, NVP possible	No data
	Dose	<b>Do not coadminister.</b>	Standard doses	<b>Do not coadminister.</b>	Standard doses
RPV	PK Data	<b>No data</b>	<u>With DTG 50 mg Once Daily:</u> • DTG AUC ↔ and C <sub>min</sub> ↑ 22% • RPV AUC ↔ and C <sub>min</sub> ↑ 21%	↑ or ↓ EVG, COBI, RPV possible	↔ RPV RAL C <sub>min</sub> ↑ 27%
	Dose	<b>Standard doses</b>	Standard doses	<b>Do not coadminister.</b>	Standard doses
PIs					
ATV/c	PK Data	<b>BIC AUC ↑ 305%</b>	No data	No data	No data
	Dose	<b>Do not coadminister.</b>	Standard doses	<b>Do not coadminister.</b>	Standard doses
ATV +/- RTV	PK Data	<b>BIC AUC ↑ 310%</b>	<u>Unboosted ATV plus DTG 30 mg Once Daily:</u> • DTG AUC ↑ 91% and C <sub>min</sub> ↑ 180%  <u>(ATV 300 mg plus RTV 100 mg) Once Daily plus DTG 30 mg Once Daily:</u> • DTG AUC ↑ 62% and C <sub>min</sub> ↑ 121%	↑ or ↓ EVG, COBI, ATV possible	<u>With Unboosted ATV:</u> • RAL AUC ↑ 72%  <u>With Unboosted ATV and RAL 1200 mg:</u> • RAL AUC ↑ 67%  <u>With (ATV 300 mg plus RTV 100 mg) Once Daily:</u> • RAL AUC ↑ 41%
	Dose	<b>Do not coadminister.</b>	Standard doses	<b>Do not coadminister.</b>	Standard doses
DRV/c	PK Data	<b>BIC AUC ↑ 74%</b>	<b><u>DRV/c plus DTG Once Daily:</u></b> • ↔ DTG, DRV, COBI  <u>DTG 50 mg Once Daily and DRV/r Once Daily Switched to DRV/c:</u> • DTG C <sub>min</sub> ↑ 100%	<u>DRV/c plus EVG/c:</u> • ↓ EVG possible	No data
	Dose	<b>Standard doses</b>	Standard doses	<b>Do not coadminister.</b>	Standard doses

**Table 20b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 3 of 3)

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
PIs, continued					
DRV/r	PK Data	No data	(DRV 600 mg plus RTV 100 mg) BID with DTG 30 mg Once Daily: • DTG AUC ↓ 22% and C <sub>min</sub> ↓ 38%	↑ or ↓ EVG, COBI, DRV possible	With (DRV 600 mg plus RTV 100 mg) BID: • RAL AUC ↓ 29% and C <sub>min</sub> ↑ 38%
	Dose	Standard doses	Standard doses	Do not coadminister.	Standard doses
LPV/r	PK Data	No data	With (LPV 400 mg plus RTV 100 mg) BID and DTG 30 mg Once Daily: • ↔ DTG	↑ or ↓ EVG, COBI, LPV possible  RTV and COBI have similar effects on CYP3A.	↓ RAL ↔ LPV/r
	Dose	Consider alternative combination.	Standard doses	Do not coadminister.	Standard doses
TPV/r	PK Data	↓ BIC possible	With (TPV 500 mg plus RTV 200 mg) BID and DTG 50 mg Once Daily: • DTG AUC ↓ 59% and C <sub>min</sub> ↓ 76%	↑ or ↓ EVG, COBI, TPV possible  RTV and COBI have similar effects on CYP3A.	With (TPV 500 mg plus RTV 200 mg) BID and RAL 400 mg BID: • RAL AUC ↓ 24% and C <sub>min</sub> ↓ 55%
	Dose	Do not coadminister.	In Patients Without INSTI Resistance: • DTG 50 mg BID  In Patients With Certain INSTI-Associated Resistance <sup>a</sup> or Clinically Suspected INSTI Resistance: • Consider alternative combination.	Do not coadminister.	RAL 400 mg BID  Coadministration with RAL 1200 mg once daily is not recommended.

<sup>a</sup> Refer to DTG product labeling for details.

**Key to Symbols:**

- ↑ = increase
- ↓ = decrease
- ↔ = no change

**Key to Acronyms:** ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; BID = twice daily; 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. Characteristics of Nucleoside Reverse Transcriptase Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 1 of 6)

Generic Name (Abbreviation) Trade Name	Formulations	Dosing Recommendations <sup>a</sup>	Elimination/ Metabolic Pathway	Serum/ Intracellular Half-Lives	Adverse Events <sup>b</sup>
<b>Abacavir</b> (ABC) <i>Ziagen</i>  <b>Note:</b> Generic tablet formulation is available.	<u>Ziagen:</u> • 300 mg tablet • 20 mg/mL oral solution	<u>Ziagen:</u> • 600 mg once daily, or • 300 mg BID  Take without regard to meals.	Metabolized by alcohol dehydrogenase and glucuronyl transferase  Renal excretion of metabolites: 82%	1.5 hours/ 12–26 hours	<ul style="list-style-type: none"> <li>• HSRs: Patients who test positive for HLA-B*5701 are at highest risk. HLA screening should be done before initiation of ABC.</li> <li>• For patients with a history of HSR, re challenge <b>is not recommended</b>.</li> <li>• Symptoms of HSR may include fever, rash, nausea, vomiting, diarrhea, abdominal pain, malaise, fatigue, or respiratory symptoms such as sore throat, cough, or shortness of breath.</li> <li>• Some cohort studies suggest increased risk of MI with recent or current use of ABC, but this risk is not substantiated in other studies.</li> </ul>
(ABC/3TC) <i>Epzicom</i>  <b>Note:</b> Generic formulation is available.	<u>Epzicom:</u> • (ABC 600 mg plus 3TC 300 mg) tablet	<u>Epzicom:</u> • 1 tablet once daily	Dose adjustment for ABC is recommended in patients with hepatic insufficiency (see <a href="#">Appendix B, Table 8</a> ).		
(ABC/DTG/3TC) <i>Triumeq</i>	<u>Triumeq:</u> • (ABC 600 mg plus 3TC 300 mg plus DTG 50 mg) tablet	<u>Triumeq:</u> • 1 tablet once daily			
(ABC/ZDV/3TC) <i>Trizivir</i>  <b>Note:</b> Generic formulation is available.	<u>Trizivir:</u> • (ABC 300 mg plus ZDV 300 mg plus 3TC 150 mg) tablet	<u>Trizivir:</u> • 1 tablet BID			
<b>Didanosine</b> (ddl) <i>Videx</i> <i>Videx EC</i>  <b>Note:</b> Generic is available as delayed-release capsules; dose is the same as Videx EC.	<u>Videx EC:</u> • 125, 200, 250, and 400 mg capsules  <u>Videx:</u> • 10 mg/mL oral solution	<p><u>Body Weight ≥60 kg:</u></p> <ul style="list-style-type: none"> <li>• ddl 400 mg once daily</li> </ul> <p><i>With TDF:</i></p> <ul style="list-style-type: none"> <li>• ddl 250 mg once daily</li> </ul> <p><u>Body Weight &lt;60 kg:</u></p> <ul style="list-style-type: none"> <li>• ddl 250 mg once daily</li> </ul> <p><i>With TDF:</i></p> <ul style="list-style-type: none"> <li>• ddl 200 mg once daily</li> </ul> <p>Take 1/2 hour before or 2 hours after a meal.</p> <p><b>Note:</b> Preferred dosing with oral solution is BID (with the total daily dose divided into 2 doses).</p>			

**Appendix B, Table 1. Characteristics of Nucleoside Reverse Transcriptase Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 2 of 6)

Generic Name (Abbreviation) Trade Name	Formulations	Dosing Recommendations <sup>a</sup>	Elimination/ Metabolic Pathway	Serum/ Intracellular Half-Lives	Adverse Events <sup>b</sup>
<b>Emtricitabine</b> (FTC) <i>Emtriva</i>	<u>Emtriva:</u> • 200 mg hard gelatin capsule • 10 mg/mL oral solution	<u>Emtriva</u> <i>Capsule:</i> • FTC 200 mg once daily  <i>Oral Solution:</i> • FTC 240 mg (24 mL) once daily  Take without regard to meals.	Renal excretion: 86%  Dose adjustment is recommended in patients with renal insufficiency (see <a href="#">Appendix B, Table 8</a> ).	10 hours/ >20 hours	<ul style="list-style-type: none"> <li>Minimal toxicity</li> <li>Hyperpigmentation/skin discoloration</li> <li>Severe acute exacerbation of hepatitis may occur in HBV coinfecting patients who discontinue FTC.</li> </ul>
(FTC/TAF) <i>Descovy</i>	<u>Descovy:</u> • (FTC 200 mg plus TAF 25 mg) tablet	<u>Descovy:</u> • 1 tablet once daily			
(FTC/TDF) <i>Truvada</i>	<u>Truvada:</u> • (FTC 200 mg plus TDF 300 mg) tablet	<u>Truvada:</u> • 1 tablet once daily			
(FTC/BIC/TAF) <i>Biktarvy</i>	<u>Biktarvy:</u> • (FTC 200 mg plus BIC 50 mg plus TAF 25 mg) tablet	<u>Biktarvy:</u> • 1 tablet once daily			
(FTC/DRV/c/TAF) <i>Symtuza</i>	<u>Symtuza:</u> • (FTC 200 mg plus DRV 800 mg plus COBI 150 mg plus TAF 10 mg) tablet	<u>Symtuza:</u> • 1 tablet once daily with food			
(FTC/EFV/TDF) <i>Atripla</i>	<u>Atripla:</u> • (FTC 200 mg plus EFV 600 mg plus TDF 300 mg) tablet	<u>Atripla:</u> • 1 tablet once daily on an empty stomach, preferably at bedtime			
(FTC/EVG/c/TAF) <i>Genvoya</i>	<u>Genvoya:</u> • (FTC 200 mg plus EVG 150 mg plus COBI 150 mg plus TAF 10 mg) tablet	<u>Genvoya:</u> • 1 tablet once daily with food			
(FTC/EVG/c/TDF) <i>Stribild</i>	<u>Stribild:</u> • (FTC 200 mg plus EVG 150 mg plus COBI 150 mg plus TDF 300 mg) tablet	<u>Stribild:</u> • 1 tablet once daily with food			
(FTC/RPV/TDF) <i>Complera</i>	<u>Complera:</u> • (FTC 200 mg plus RPV 25 mg plus TDF 300 mg) tablet	<u>Complera:</u> • 1 tablet once daily with a meal			

**Appendix B, Table 1. Characteristics of Nucleoside Reverse Transcriptase Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 3 of 6)

Generic Name (Abbreviation) Trade Name	Formulations	Dosing Recommendations <sup>a</sup>	Elimination/ Metabolic Pathway	Serum/ Intracellular Half-Lives	Adverse Events <sup>b</sup>
<b>Lamivudine</b> (3TC) <i>Epivir</i>  <b>Note:</b> Generic is available.	<u>Epivir:</u> • 150 and 300 mg tablets • 10 mg/mL oral solution	<u>Epivir:</u> • 3TC 300 mg once daily, or • 3TC 150 mg BID	Renal excretion: 70%  Dose adjustment in patients with renal insufficiency is recommended (see <a href="#">Appendix B, Table 8</a> ).	5–7 hours/ 18–22 hours	• Minimal toxicity • Severe acute exacerbation of hepatitis may occur in HBV coinfecting patients who discontinue 3TC.
(3TC/ABC) <i>Epzicom</i>  <b>Note:</b> Generic is available.	<u>Epzicom:</u> • (3TC 300 mg plus ABC 600 mg) tablet	<u>Epzicom:</u> • 1 tablet once daily			
(3TC/TDF) <i>Cimduo</i>	<u>Cimduo:</u> • (3TC 300 mg plus TDF 300 mg) tablet	<u>Cimduo:</u> • 1 tablet once daily			
(3TC/ZDV) <i>Combivir</i>  <b>Note:</b> Generic is available.	<u>Combivir:</u> • (3TC 150 mg plus ZDV 300 mg) tablet	<u>Combivir:</u> • 1 tablet BID			
(3TC/ABC/ZDV) <i>Trizivir</i>  <b>Note:</b> Generic is available.	<u>Trizivir:</u> • (3TC 150 mg plus ZDV 300 mg plus ABC 300 mg) tablet	<u>Trizivir:</u> • 1 tablet BID			
(3TC/DOR/TDF) <i>Delstrigo</i>	<u>Delstrigo:</u> • (3TC 300 mg plus DOR 100 mg plus TDF 300 mg) tablet	<u>Delstrigo:</u> • 1 tablet once daily			
(3TC/DTG/ABC) <i>Triumeq</i>	<u>Triumeq:</u> • (3TC 300 mg plus ABC 600 mg plus DTG 50 mg) tablet	<u>Triumeq:</u> • 1 tablet once daily			
(3TC/EFV/TDF) <i>Symfi</i>	<u>Symfi:</u> • (3TC 300 mg plus EFV 600 mg plus TDF 300 mg) tablet	<u>Symfi:</u> • 1 tablet once daily on an empty stomach, preferably at bedtime			
(3TC/EFV/TDF) <i>Symfi Lo</i>	<u>Symfi Lo:</u> • (3TC 300 mg plus EFV 400 mg plus TDF 300 mg) tablet	<u>Symfi Lo:</u> • 1 tablet once daily on an empty stomach, preferably at bedtime			

**Appendix B, Table 1. Characteristics of Nucleoside Reverse Transcriptase Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 4 of 6)

Generic Name (Abbreviation) Trade Name	Formulations	Dosing Recommendations <sup>a</sup>	Elimination/ Metabolic Pathway	Serum/ Intracellular Half-Lives	Adverse Events <sup>b</sup>
<b>Stavudine</b> (d4T) <i>Zerit</i>  <b>Note:</b> Generic is available.	<u>Zerit:</u> • 15, 20, 30, and 40 mg capsules • 1 mg/mL oral solution	<u>Body Weight ≥60 kg:</u> • d4T 40 mg BID  <u>Body Weight &lt;60 kg:</u> • d4T 30 mg BID  Take without regard to meals.  <b>Note:</b> WHO recommends 30 mg BID dosing regardless of body weight.	Renal excretion: 50%  Dose adjustment is recommended in patients with renal insufficiency (see <a href="#">Appendix B, Table 8</a> ).	1 hour/ 7.5 hours	<ul style="list-style-type: none"> <li>Peripheral neuropathy</li> <li>Lipoatrophy</li> <li>Pancreatitis</li> <li>Lactic acidosis/severe hepatomegaly with hepatic steatosis (rare but potentially life-threatening toxicity)</li> <li>Hyperlipidemia</li> <li>Insulin resistance/diabetes mellitus</li> <li>Rapidly progressive ascending neuromuscular weakness (rare)</li> </ul>
<b>Tenofovir Alafenamide</b> (TAF) <i>Vemlidy</i>  <b>Note:</b> Available as a 25-mg tablet for the treatment of HBV.	See FDCs for HIV treatment below.	See FDCs for HIV treatment below.	Metabolized by cathepsin A.  Not recommended in patients with CrCl <30 mL/min.	0.5 hours/ 150–180 hours	<ul style="list-style-type: none"> <li>Renal insufficiency, Fanconi syndrome, proximal renal tubulopathy are less likely to occur with TAF than with TDF.</li> <li>Osteomalacia, decrease in bone mineral density are less likely to occur with TAF than with TDF.</li> <li>Severe acute exacerbation of hepatitis may occur in HBV coinfecting patients who discontinue TAF.</li> <li>Diarrhea, nausea, headache</li> </ul>
(FTC/TAF) <i>Descovy</i>	<u>Descovy:</u> • (FTC 200 mg plus TAF 25 mg) tablet	<u>Descovy:</u> • 1 tablet once daily			
(TAF/BIC/FTC) <i>Biktarvy</i>	<u>Biktarvy:</u> • (TAF 25 mg plus BIC 50 mg plus FTC 200 mg) tablet	<u>Biktarvy:</u> • 1 tablet once daily			
(TAF/DRV/c/FTC) <i>Symtuza</i>	<u>Symtuza:</u> • (TAF 10 mg plus DRV 800 mg plus COBI 150 mg plus FTC 200 mg) tablet	<u>Symtuza:</u> • 1 tablet once daily with food			
(TAF/EVG/c/FTC) <i>Genvoya</i>	<u>Genvoya:</u> • (TAF 10 mg plus EVG 150 mg plus COBI 150 mg plus FTC 200 mg) tablet	<u>Genvoya:</u> • 1 tablet once daily with food			
(TAF/RPV/FTC) <i>Odefsey</i>	<u>Odefsey:</u> • (TAF 25 mg plus RPV 25 mg plus FTC 200 mg) tablet	<u>Odefsey:</u> • 1 tablet once daily with a meal			

**Appendix B, Table 1. Characteristics of Nucleoside Reverse Transcriptase Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 5 of 6)

Generic Name (Abbreviation) Trade Name	Formulations	Dosing Recommendations <sup>a</sup>	Elimination/ Metabolic Pathway	Serum/ Intracellular Half-Lives	Adverse Events <sup>b</sup>
<b>Tenofovir Disoproxil Fumarate</b> (TDF) <i>Viread</i>  <b>Note: Generic is available.</b>	<u>Viread:</u> • 150, 200, 250, and 300 mg tablets • 40 mg/g oral powder  <u>Generic:</u> • 300 mg tablet	<u>Viread:</u> • TDF 300 mg once daily, <i>or</i> • 7.5 level scoops of oral powder once daily (dosing scoop dispensed with each prescription; 1 level scoop contains 1g of oral powder).  • Take without regard to meals.  Mix oral powder with 2–4 ounces of a soft food that does not require chewing (e.g., applesauce, yogurt). <b>Do not mix oral powder with liquid.</b>	Renal excretion is primary route of elimination.  Dose adjustment is recommended in patients with renal insufficiency (see <a href="#">Appendix B, Table 8</a> ).	17 hours/ >60 hours	<ul style="list-style-type: none"> <li>Renal insufficiency, Fanconi syndrome, proximal renal tubulopathy</li> <li>Osteomalacia, decrease in bone mineral density</li> <li>Severe acute exacerbation of hepatitis may occur in HBV-coinfected patients who discontinue TDF.</li> <li>Asthenia, headache, diarrhea, nausea, vomiting, and flatulence</li> </ul>
(TDF/3TC) <i>Cimduo</i>	<u>Cimduo:</u> • (TDF 300 mg plus 3TC 300 mg) tablet	<u>Cimduo:</u> • 1 tablet once daily			
(TDF/FTC) <i>Truvada</i>	<u>Truvada:</u> • (TDF 300 mg plus FTC 200 mg) tablet	<u>Truvada:</u> • 1 tablet once daily • Take without regard to meals.			
(TDF/DOR/3TC) <i>Delstrigo</i>	<u>Delstrigo:</u> • (TDF 300 mg plus DOR 100 mg plus 3TC 300 mg) tablet	<u>Delstrigo:</u> • 1 tablet once daily			
(TDF/EFV/FTC) <i>Atripla</i>	<u>Atripla:</u> • (TDF 300 mg plus EFV 600 mg plus FTC 200 mg) tablet	<u>Atripla:</u> • 1 tablet once daily on an empty stomach, preferably at bedtime			
(TDF/EFV/3TC) <i>Symfi</i>	<u>Symfi:</u> • (TDF 300 mg plus EFV 600 mg plus 3TC 300 mg) tablet	<u>Symfi:</u> • 1 tablet once daily on an empty stomach, preferably at bedtime			
(TDF/EFV/3TC) <i>Symfi Lo</i>	<u>Symfi Lo:</u> • (TDF 300 mg plus EFV 400 mg plus 3TC 300 mg) tablet	<u>Symfi Lo:</u> • 1 tablet once daily on an empty stomach, preferably at bedtime			
(TDF/EVG/c/FTC) <i>Stribild</i>	<u>Stribild:</u> • (TDF 300 mg plus EVG 150 mg plus COBI 150 mg plus FTC 200 mg) tablet	<u>Stribild:</u> • 1 tablet once daily • Take with food.			
(TDF/RPV/FTC) <i>Complera</i>	<u>Complera:</u> • (TDF 300 mg plus RPV 25 mg plus FTC 200 mg) tablet	<u>Complera:</u> • 1 tablet once daily • Take with a meal.			



**Appendix B, Table 1. Characteristics of Nucleoside Reverse Transcriptase Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 6 of 6)

Generic Name (Abbreviation) Trade Name	Formulations	Dosing Recommendations <sup>a</sup>	Elimination/ Metabolic Pathway	Serum/ Intracellular Half-Lives	Adverse Events <sup>b</sup>
<b>Zidovudine</b> (ZDV) <i>Retrovir</i>  <b>Note:</b> Generic is available.	<u>Retrovir:</u> • 100 mg capsule • 300 mg tablet (only available as generic) • 10 mg/mL intravenous solution • 10 mg/mL oral solution	<u>Retrovir:</u> • ZDV 300 mg BID, <i>or</i> • ZDV 200 mg TID • Take without regard to meals.	Metabolized to GAZT  Renal excretion of GAZT  Dose adjustment is recommended in patients with renal insufficiency (see <a href="#">Appendix B, Table 8</a> ).	1.1 hours/ 7 hours	<ul style="list-style-type: none"> <li>• Bone marrow suppression: macrocytic anemia or neutropenia</li> <li>• Nausea, vomiting, headache, insomnia, asthenia</li> <li>• Nail pigmentation</li> <li>• Lactic acidosis/severe hepatomegaly with hepatic steatosis (rare but potentially life-threatening toxicity)</li> <li>• Hyperlipidemia</li> <li>• Insulin resistance/diabetes mellitus</li> <li>• Lipoatrophy</li> <li>• Myopathy</li> </ul>
(ZDV/3TC) <i>Combivir</i>  <b>Note:</b> Generic is available.	<u>Combivir:</u> • (ZDV 300 mg plus 3TC 150 mg) tablet	<u>Combivir:</u> • 1 tablet BID • Take without regard to meals.			
(ZDV/3TC/ABC) <i>Trizivir</i>  <b>Note:</b> Generic is available.	<u>Trizivir:</u> • (ZDV 300 mg plus 3TC 150 mg plus ABC 300 mg) tablet	<u>Trizivir:</u> • 1 tablet BID • Take without regard to meals.			

<sup>a</sup> For dose adjustments in patients with renal or hepatic insufficiency, see [Appendix B, Table 8](#).

<sup>b</sup> Also see [Table 15](#).

**Key to Acronyms:** 3TC = lamivudine; ABC = abacavir; **BIC = bicitegravir**; BID = twice daily; COBI = cobicistat; CrCl = creatinine clearance; d4T = stavudine; ddl = didanosine; **DOR = doravirine**; DRV = darunavir; DTG = dolutegravir; EC = enteric coated; EFV = efavirenz; EVG = elvitegravir; FDC = fixed-dose combination; FTC = emtricitabine; GAZT = azidothymidine glucuronide; HBV = hepatitis B virus; HLA = human leukocyte antigen; HSR = hypersensitivity reaction; MI = myocardial infarction; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TID = three times a day; WHO = World Health Organization; ZDV = zidovudine

**Appendix B, Table 2. Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 1 of 2)

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

Generic Name (Abbreviation) Trade Name	Formulations	Dosing Recommendations <sup>a</sup>	Elimination/Metabolic Pathway	Serum Half-Life	Adverse Events <sup>b</sup>
<b>Doravirine</b> (DOR) <i>Pifeltro</i>	<u>Pifeltro:</u> • 100 mg tablet	<u>Pifeltro:</u> • 1 tablet once daily	CYP3A4/5 substrate	15 hours	<ul style="list-style-type: none"> <li>• Nausea</li> <li>• Dizziness</li> <li>• Abnormal dreams</li> </ul>
(DOR/TDF/3TC) <i>Delstrigo</i>	<u>Delstrigo:</u> • (DOR 100 mg plus TDF 300 mg plus 3TC 300 mg) tablet	<u>Delstrigo:</u> • 1 tablet once daily			
<b>Efavirenz</b> (EFV) <i>Sustiva</i>	<u>Sustiva:</u> • 50 and 200 mg capsules • 600 mg tablet <u>Generic:</u> • 600 mg tablet	<u>Sustiva:</u> • 600 mg once daily, at or before bedtime • Take on an empty stomach to reduce side effects.	Metabolized by CYPs 2B6 (primary), 3A4, and 2A6  CYP3A4 mixed inducer/inhibitor (more an inducer than an inhibitor) CYP2C9 and 2C19 inhibitor; 2B6 inducer	40–55 hours	<ul style="list-style-type: none"> <li>• Rash<sup>e</sup></li> <li>• Neuropsychiatric symptoms<sup>d</sup></li> <li>• Increased transaminase levels</li> <li>• Hyperlipidemia</li> <li>• False-positive results with some cannabinoid and benzodiazepine screening assays reported</li> <li>• QT interval prolongation</li> </ul>
<b>Note:</b> Generic product is available.					
(EFV/TDF/FTC) <i>Atripla</i>	<u>Atripla:</u> • (EFV 600 mg plus TDF 300 mg plus FTC 200 mg) tablet	<u>Atripla:</u> • 1 tablet once daily on an empty stomach, preferably at bedtime			
(EFV/TDF/3TC) <i>Symfi</i>	<u>Symfi:</u> • (EFV 600 mg plus TDF 300 mg plus 3TC 300 mg) tablet	<u>Symfi:</u> • 1 tablet once daily on an empty stomach, preferably at bedtime			
(EFV/TDF/3TC) <i>Symfi Lo</i>	<u>Symfi Lo:</u> • (EFV 400 mg plus TDF 300 mg plus 3TC 300 mg) tablet	<u>Symfi Lo:</u> • 1 tablet once daily on an empty stomach, preferably at bedtime			
<b>Etravirine</b> (ETR) <i>Intence</i>	<u>Intence:</u> • 25, 100, and 200 mg tablets	<u>Intence:</u> • 200 mg BID • Take following a meal.	CYP3A4, 2C9, and 2C19 substrate  3A4 inducer; 2C9 and 2C19 inhibitor	41 hours	<ul style="list-style-type: none"> <li>• Rash, including Stevens-Johnson syndrome<sup>e</sup></li> <li>• HSRs, characterized by rash, constitutional findings, and sometimes organ dysfunction (including hepatic failure) have been reported.</li> <li>• Nausea</li> </ul>

**Appendix B, Table 2. Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 2 of 2)

Generic Name (Abbreviation) Trade Name	Formulations	Dosing Recommendations <sup>a</sup>	Elimination/Metabolic Pathway	Serum Half-Life	Adverse Events <sup>b</sup>
<b>Nevirapine</b> (NVP) <i>Viramune</i> or <i>Viramune XR</i>  <b>Note:</b> Generic is available for 200 mg tablets and oral suspension.	<ul style="list-style-type: none"> <li>• 200 mg tablet</li> <li>• 400 mg XR tablet</li> <li>• 50 mg/5 mL oral suspension</li> </ul>	<ul style="list-style-type: none"> <li>• 200 mg once daily for 14 days (lead-in period); thereafter, 200 mg BID, or 400 mg (Viramune XR tablet) once daily</li> <li>• Take without regard to meals.</li> <li>• Repeat lead-in period if therapy is discontinued for &gt;7 days.</li> <li>• In patients who develop mild-to-moderate rash without constitutional symptoms, continue lead-in period until rash resolves, but do not administer for longer than 28 days total.</li> </ul>	CYP450 substrate, inducer of 3A4 and 2B6; 80% excreted in urine (glucuronidated metabolites, <5% unchanged); 10% in feces  Contraindicated in patients with moderate to severe hepatic impairment.  Dose adjustment is recommended in patients on hemodialysis (see <a href="#">Appendix B, Table 8</a> ).	25–30 hours	<ul style="list-style-type: none"> <li>• Rash, including Stevens-Johnson syndrome<sup>c</sup></li> <li>• Symptomatic hepatitis, including fatal hepatic necrosis, has been reported:               <ul style="list-style-type: none"> <li>• Rash reported in approximately 50% of cases.</li> <li>• Occurs at significantly higher frequency in ARV-naive female patients with pre-NVP CD4 counts &gt;250 cells/mm<sup>3</sup> and in ARV-naive male patients with pre-NVP CD4 counts &gt;400 cells/mm<sup>3</sup>. NVP should not be initiated in these patients unless the benefit clearly outweighs the risk.</li> </ul> </li> </ul>
<b>Rilpivirine</b> (RPV) <i>Edurant</i>	<b>Edurant:</b> <ul style="list-style-type: none"> <li>• 25 mg tablet</li> </ul>	<b>Edurant:</b> <ul style="list-style-type: none"> <li>• 25 mg once daily</li> <li>• Take with a meal.</li> </ul>	CYP3A4 substrate	50 hours	<ul style="list-style-type: none"> <li>• Rash<sup>c</sup></li> <li>• Depression, insomnia, headache</li> <li>• Hepatotoxicity</li> <li>• QT interval prolongation</li> </ul>
(RPV/DTG) <i>Juluca</i>	<b>Juluca:</b> <ul style="list-style-type: none"> <li>• (RPV 25 mg plus DTG 50 mg) tablet</li> </ul>	<b>Juluca:</b> <ul style="list-style-type: none"> <li>• 1 tablet once daily</li> <li>• Take with a meal.</li> </ul>			
(RPV/TAF/FTC) <i>Odefsey</i>	<b>Odefsey:</b> <ul style="list-style-type: none"> <li>• (RPV 25 mg plus TAF 25 mg plus FTC 200 mg) tablet</li> </ul>	<b>Odefsey:</b> <ul style="list-style-type: none"> <li>• 1 tablet once daily</li> <li>• Take with a meal.</li> </ul>			
(RPV/TDF/FTC) <i>Complera</i>	<b>Complera:</b> <ul style="list-style-type: none"> <li>• (RPV 25 mg plus TDF 300 mg plus FTC 200 mg) tablet</li> </ul>	<b>Complera:</b> <ul style="list-style-type: none"> <li>• 1 tablet once daily</li> <li>• Take with a meal.</li> </ul>			

<sup>a</sup> For dose adjustments in patients with renal or hepatic insufficiency, see [Appendix B, Table 8](#).

<sup>b</sup> Also see [Table 15](#).

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

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

**Key to Acronyms:** 3TC = lamivudine; ARV = antiretroviral; BID = twice daily; CD4 = CD4 T lymphocyte; CYP = cytochrome P; DLV = delavirdine; DOR = doravirine; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; FTC = emtricitabine; HSR = hypersensitivity reaction; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; XR = extended release

**Appendix B, Table 3. Characteristics of Protease Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 1 of 6)

Generic Name (Abbreviation) Trade Name	Formulations	Dosing Recommendations <sup>a</sup>	Elimination/Metabolic Pathway	Serum Half-Life	Adverse Events <sup>b</sup>
<b>Atazanavir</b> (ATV) <i>Reyataz</i>  <b>Note: Generic is available for capsule formulations.</b>	<u>Reyataz:</u> <ul style="list-style-type: none"> <li>• 150, 200, and 300 mg capsules</li> <li>• 50 mg single packet oral powder</li> </ul>	<u>In ARV-Naive Patients:</u> <ul style="list-style-type: none"> <li>• (ATV 300 mg plus RTV 100 mg) once daily; <i>or</i></li> <li>• ATV 400 mg once daily</li> </ul> <u>With TDF or in ARV-Experienced Patients:</u> <ul style="list-style-type: none"> <li>• (ATV 300 mg plus RTV 100 mg) once daily</li> </ul> <u>With EFV in ARV-Naive Patients:</u> <ul style="list-style-type: none"> <li>• (ATV 400 mg plus RTV 100 mg) once daily</li> </ul> Take with food.  For dosing recommendations with H2 antagonists and PPIs, refer to <a href="#">Table 19a</a> .	CYP3A4 inhibitor and substrate; weak CYP2C8 inhibitor; UGT1A1 inhibitor  Dose adjustment is recommended in patients with hepatic insufficiency (see <a href="#">Appendix B, Table 8</a> ).	7 hours	<ul style="list-style-type: none"> <li>• Indirect hyperbilirubinemia</li> <li>• PR interval prolongation: First degree symptomatic AV block reported. Use with caution in patients who have underlying conduction defects or who are on concomitant medications that can cause PR prolongation.</li> <li>• Hyperglycemia</li> <li>• Fat maldistribution</li> <li>• Cholelithiasis</li> <li>• Nephrolithiasis</li> <li>• Renal insufficiency</li> <li>• Serum transaminase elevations</li> <li>• Hyperlipidemia (especially with RTV boosting)</li> <li>• Skin rash</li> <li>• Increase in serum creatinine (with COBI)</li> </ul>
(ATV/c) <i>Evotaz</i>	<u>Evotaz:</u> <ul style="list-style-type: none"> <li>• (ATV 300 mg plus COBI 150 mg) tablet</li> </ul>	<u>Evotaz:</u> <ul style="list-style-type: none"> <li>• 1 tablet once daily</li> <li>• Take with food.</li> </ul> <u>With TDF:</u> <ul style="list-style-type: none"> <li>• <b>Not recommended</b> for patients with baseline CrCl &lt;70 mL/min (see <a href="#">Appendix B, Table 8</a> for the equation for calculating CrCl).</li> </ul>	ATV: as above  COBI: CYP3A inhibitor and substrate; CYP2D6 inhibitor		

**Appendix B, Table 3. Characteristics of Protease Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 2 of 6)

Generic Name (Abbreviation) Trade Name	Formulations	Dosing Recommendations <sup>a</sup>	Elimination/Metabolic Pathway	Serum Half-Life	Adverse Events <sup>b</sup>
Darunavir (DRV) Prezista	Prezista: • 75, 150, 600, and 800 mg tablets • 100 mg/ mL oral suspension	<u>In ARV-Naive Patients or ARV- Experienced Patients with No DRV Mutations:</u> • (DRV 800 mg plus RTV 100 mg) once daily  <u>In ARV-Experienced Patients with One or More DRV Resistance Mutations:</u> • (DRV 600 mg plus RTV 100 mg) BID  Unboosted DRV is <b>not recommended</b> .  Take with food.	CYP3A4 inhibitor and substrate; CYP2C9 inducer	15 hours (when combined with RTV)	• Skin rash (10%): DRV has a sulfonamide moiety; Stevens-Johnson syndrome, toxic epidermal necrolysis, acute generalized exanthematous pustulosis, and erythema multiforme have been reported. • Hepatotoxicity • Diarrhea, nausea • Headache • Hyperlipidemia • Serum transaminase elevation
(DRV/c) Prezcobix	Prezcobix: • (DRV 800 mg plus COBI 150 mg) tablet	Prezcobix: • 1 tablet once daily • Take with food.  <b>Not recommended</b> for patients with 1 or more DRV resistance- associated mutations.  With TDF: • <b>Not recommended</b> for patients with baseline CrCl <70 mL/min (see <a href="#">Appendix B, Table 8</a> for the equation for calculating CrCl).	DRV: CYP3A4 inhibitor and substrate; CYP2C9 inducer  COBI: CYP3A inhibitor and substrate; CYP2D6 inhibitor	<b>7 hours</b> (when combined with COBI)	• Hyperglycemia • Fat maldistribution • Increase in serum creatinine (with COBI)
(DRV/c/TAF/ FTC) Symtuza	Symtuza: • (DRV 800 mg plus COBI 150 mg plus TAF 10 mg plus FTC 200 mg) tablet	Symtuza: • 1 tablet once daily with food  <b>Not recommended</b> for patients with 1 or more DRV resistance- associated mutations.  <b>Not recommended</b> for patients with CrCl <30 mL/min.  <b>Not recommended</b> in patients with severe hepatic impairment.	DRV: CYP3A4 inhibitor and substrate; CYP2C9 inducer  COBI: CYP3A inhibitor and substrate; CYP2D6 inhibitor		

**Appendix B, Table 3. Characteristics of Protease Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 3 of 6)

Generic Name (Abbreviation) Trade Name	Formulations	Dosing Recommendations <sup>a</sup>	Elimination/Metabolic Pathway	Serum Half-Life	Adverse Events <sup>b</sup>
<p><b>Fosamprenavir</b> (FPV, a prodrug of APV) <i>Lexiva</i></p> <p><b>Note:</b> Generic is available.</p>	<p><u>Lexiva:</u></p> <ul style="list-style-type: none"> <li>• 700 mg tablet</li> <li>• 50 mg/mL oral suspension</li> </ul>	<p><u>In ARV-Naive Patients:</u></p> <ul style="list-style-type: none"> <li>• FPV 1400 mg BID, <i>or</i></li> <li>• (FPV 1400 mg plus RTV 100–200 mg) once daily, <i>or</i></li> <li>• (FPV 700 mg plus RTV 100 mg) BID</li> </ul> <p><u>In PI-Experienced Patients (Once-Daily Dosing <b>Not Recommended</b>):</u></p> <ul style="list-style-type: none"> <li>• (FPV 700 mg plus RTV 100 mg) BID</li> </ul> <p><u>With EFV:</u></p> <ul style="list-style-type: none"> <li>• (FPV 700 mg plus RTV 100 mg) BID, <i>or</i></li> <li>• (FPV 1400 mg plus RTV 300 mg) once daily</li> </ul> <p><u>Tablet:</u></p> <ul style="list-style-type: none"> <li>• Without RTV tablet: Take without regard to meals.</li> <li>• With RTV tablet: Take with meals.</li> </ul> <p><u>Oral Suspension:</u></p> <ul style="list-style-type: none"> <li>• Take without food.</li> </ul>	<p>APV is a CYP3A4 substrate, inhibitor, and inducer.</p> <p>Dose adjustment is recommended in patients with hepatic insufficiency (see <a href="#">Appendix B, Table 8</a>).</p>	7.7 hours (APV)	<ul style="list-style-type: none"> <li>• Skin rash (reported in 12% to 19% of patients on FPV): FPV has a sulfonamide moiety.</li> <li>• Diarrhea, nausea, vomiting</li> <li>• Headache</li> <li>• Hyperlipidemia</li> <li>• Serum transaminase elevation</li> <li>• Hyperglycemia</li> <li>• Fat maldistribution</li> <li>• Possible increase in the frequency of bleeding episodes in patients with hemophilia</li> <li>• Nephrolithiasis</li> </ul>
<p><b>Indinavir</b> (IDV) <i>Crixivan</i></p>	<p><u>Crixivan:</u></p> <ul style="list-style-type: none"> <li>• 200 and 400 mg capsules</li> </ul>	<p><u>Crixivan:</u></p> <ul style="list-style-type: none"> <li>• IDV 800 mg every 8 hours</li> <li>• Take 1 hour before or 2 hours after meals; may take with skim milk or a low-fat meal.</li> </ul> <p><u>With RTV:</u></p> <ul style="list-style-type: none"> <li>• (IDV 800 mg plus RTV 100–200 mg) BID</li> <li>• Take without regard to meals.</li> </ul> <p>Drink at least 48 oz of water daily.</p>	<p>CYP3A4 inhibitor and substrate</p> <p>Dose adjustment is recommended in patients with hepatic insufficiency (see <a href="#">Appendix B, Table 8</a>).</p>	1.5–2 hours	<ul style="list-style-type: none"> <li>• Nephrolithiasis</li> <li>• GI intolerance, nausea</li> <li>• Hepatitis</li> <li>• Indirect hyperbilirubinemia</li> <li>• Hyperlipidemia</li> <li>• Headache, asthenia, blurred vision, dizziness, rash, metallic taste, thrombocytopenia, alopecia, and hemolytic anemia</li> <li>• Hyperglycemia</li> <li>• Fat maldistribution</li> <li>• Possible increase in the frequency of bleeding episodes in patients with hemophilia</li> </ul>

**Appendix B, Table 3. Characteristics of Protease Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 4 of 6)

Generic Name (Abbreviation) Trade Name	Formulations	Dosing Recommendations <sup>a</sup>	Elimination/Metabolic Pathway	Serum Half-Life	Adverse Events <sup>b</sup>
<b>Lopinavir/ Ritonavir</b> (LPV/r) <i>Kaletra</i>	<u>Kaletra</u> <u>Tablets:</u> <ul style="list-style-type: none"> <li>• (LPV 200 mg plus RTV 50 mg), <i>or</i></li> <li>• (LPV 100 mg plus RTV 25 mg)</li> </ul> <u>Oral Solution:</u> <ul style="list-style-type: none"> <li>• Each 5 mL contains (LPV 400 mg plus RTV 100 mg).</li> <li>• Oral solution contains 42% alcohol.</li> </ul>	<u>Kaletra:</u> <ul style="list-style-type: none"> <li>• (LPV 400 mg plus RTV 100 mg) BID, <i>or</i></li> <li>• (LPV 800 mg plus RTV 200 mg) once daily</li> </ul> <p>Once-daily dosing <b>is not recommended</b> for patients with ≥3 LPV-associated mutations, pregnant women, or patients receiving EFV, NVP, FPV, NFV, carbamazepine, phenytoin, or phenobarbital.</p> <p><u>With EFV or NVP (PI-Naive or PI Experienced Patients):</u></p> <ul style="list-style-type: none"> <li>• LPV/r 500 mg/125 mg tablets BID (use a combination of 2 LPV/r 200 mg/50 mg tablets plus 1 LPV/r 100 mg/25 mg tablet to make a total dose of LPV/r 500 mg/125 mg), <i>or</i></li> <li>• LPV/r 533 mg/133 mg oral solution BID</li> </ul> <p><u>Tablet:</u></p> <ul style="list-style-type: none"> <li>• Take without regard to meals.</li> </ul> <p><u>Oral Solution:</u></p> <ul style="list-style-type: none"> <li>• Take with food.</li> </ul>	CYP3A4 inhibitor and substrate	5–6 hours	<ul style="list-style-type: none"> <li>• GI intolerance, nausea, vomiting, diarrhea</li> <li>• Pancreatitis</li> <li>• Asthenia</li> <li>• Hyperlipidemia (especially hypertriglyceridemia)</li> <li>• Serum transaminase elevation</li> <li>• Hyperglycemia</li> <li>• Insulin resistance/diabetes mellitus</li> <li>• Fat maldistribution</li> <li>• Possible increase in the frequency of bleeding episodes in patients with hemophilia</li> <li>• PR interval prolongation</li> <li>• QT interval prolongation and torsades de pointes have been reported; however, causality could not be established.</li> </ul>
<b>Nelfinavir</b> (NFV) <i>Viracept</i>	<u>Viracept:</u> <ul style="list-style-type: none"> <li>• 250 and 625 mg tablets</li> </ul>	<u>Viracept:</u> <ul style="list-style-type: none"> <li>• NFV 1250 mg BID, <i>or</i></li> <li>• NFV 750 mg TID</li> </ul> <p>Dissolve tablets in a small amount of water, mix admixture well, and consume immediately.</p> <p>Take with food.</p>	CYP2C19 and 3A4 substrate—metabolized to active M8 metabolite; CYP3A4 inhibitor	3.5–5 hours	<ul style="list-style-type: none"> <li>• Diarrhea</li> <li>• Hyperlipidemia</li> <li>• Hyperglycemia</li> <li>• Fat maldistribution</li> <li>• Possible increase in the frequency of bleeding episodes in patients with hemophilia</li> <li>• Serum transaminase elevation</li> </ul>

<sup>a</sup> Also see [Table 14](#).

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

**Appendix B, Table 3. Characteristics of Protease Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 5 of 6)

Generic Name (Abbreviation) Trade Name	Formulations	Dosing Recommendations <sup>a</sup>	Elimination/Metabolic Pathway	Serum Half-Life	Adverse Events <sup>b</sup>
<b>Ritonavir</b> (RTV) <i>Norvir</i>  <b>Note: Generic is available.</b>	<u>Norvir:</u> <ul style="list-style-type: none"> <li>• 100 mg tablet</li> <li>• 100 mg soft gel capsule</li> <li>• 80 mg/mL oral solution</li> <li>• 100 mg single packet oral powder</li> </ul> Oral solution contains 43% alcohol.	<u>As PK Booster (or Enhancer) for Other PIs:</u> <ul style="list-style-type: none"> <li>• RTV 100–400 mg per day in 1 or 2 divided doses (refer to other PIs for specific dosing recommendations).</li> </ul> <u>Tablet:</u> <ul style="list-style-type: none"> <li>• Take with food.</li> </ul> <u>Capsule and Oral Solution:</u> <ul style="list-style-type: none"> <li>• To improve tolerability, take with food if possible.</li> </ul>	CYP3A4 > 2D6 substrate; potent 3A4, 2D6 inhibitor; inducer of UGT1A1 and CYPs 1A2, 2C8, 2C9, and 2C19	3–5 hours	<ul style="list-style-type: none"> <li>• GI intolerance, nausea, vomiting, diarrhea</li> <li>• Paresthesia (circumoral and extremities)</li> <li>• Hyperlipidemia (especially hypertriglyceridemia)</li> <li>• Hepatitis</li> <li>• Asthenia</li> <li>• Taste perversion</li> <li>• Hyperglycemia</li> <li>• Fat maldistribution</li> <li>• Possible increase in the frequency of bleeding episodes in patients with hemophilia</li> </ul>
<b>Saquinavir</b> (SQV) <i>Invirase</i>	<u>Invirase:</u> <ul style="list-style-type: none"> <li>• 500 mg tablet</li> <li>• 200 mg capsule</li> </ul>	<u>Invirase:</u> <ul style="list-style-type: none"> <li>• (SQV 1000 mg plus RTV 100 mg) BID</li> </ul> Unboosted SQV is <b>not recommended</b> .  Take with meals or within 2 hours after a meal.	CYP3A4 substrate	1–2 hours	<ul style="list-style-type: none"> <li>• GI intolerance, nausea, and diarrhea</li> <li>• Headache</li> <li>• Serum transaminase elevation</li> <li>• Hyperlipidemia</li> <li>• Hyperglycemia</li> <li>• Fat maldistribution</li> <li>• Possible increase in the frequency of bleeding episodes in patients with hemophilia</li> <li>• PR interval prolongation</li> <li>• QT interval prolongation, torsades de pointes have been reported. Patients with pre-SQV QT interval &gt;450 msec should not receive SQV.</li> </ul>



**Appendix B, Table 3. Characteristics of Protease Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 6 of 6)

Generic Name (Abbreviation) Trade Name	Formulations	Dosing Recommendations <sup>a</sup>	Elimination/Metabolic Pathway	Serum Half-Life	Adverse Events <sup>b</sup>
<b>Tipranavir</b> (TPV) <i>Aptivus</i>	<u>Aptivus:</u> <ul style="list-style-type: none"> <li>• 250 mg capsule</li> <li>• 100 mg/mL oral solution</li> </ul>	<u>Aptivus:</u> <ul style="list-style-type: none"> <li>• (TPV 500 mg plus RTV 200 mg) BID</li> </ul> <p>Unboosted TPV is <b>not recommended.</b></p> <p><u>With RTV Tablets:</u></p> <ul style="list-style-type: none"> <li>• Take with meals.</li> </ul> <p><u>With RTV Capsules or Solution:</u></p> <ul style="list-style-type: none"> <li>• Take without regard to meals.</li> </ul>	CYP3A4 inducer and substrate  CYP2D6 inhibitor; CYP3A4, 1A2, and 2C19 inducer  Net effect of combining TPV and RTV is a CYP3A4 and 2D6 inhibitor	6 hours after single dose of TPV/r	<ul style="list-style-type: none"> <li>• Hepatotoxicity: clinical hepatitis (including hepatic decompensation and hepatitis-associated fatalities) has been reported; monitor patients closely, especially those with underlying liver diseases.</li> <li>• Skin rash: TPV has a sulfonamide moiety; use with caution in patients with known sulfonamide allergy.</li> <li>• Rare cases of fatal and nonfatal intracranial hemorrhages have been reported. Risks include brain lesion, head trauma, recent neurosurgery, coagulopathy, hypertension, alcoholism, and the use of anticoagulant or antiplatelet agents (including vitamin E).</li> <li>• Hyperlipidemia</li> <li>• Hyperglycemia</li> <li>• Fat maldistribution</li> <li>• Possible increase in the frequency of bleeding episodes in patients with hemophilia</li> </ul>

<sup>a</sup> For dose adjustments in patients with hepatic insufficiency, see [Appendix B, Table 8](#).

<sup>b</sup> Also see [Table 15](#).

**Key to Acronyms:** APV = amprenavir; ARV = antiretroviral; ATV = atazanavir; AV = atrioventricular; BID = twice daily; COBI = cobicistat; CrCl = creatinine clearance; CYP = cytochrome P; DRV = darunavir; DRV/c = darunavir/cobicistat; EFV = efavirenz; 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; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TID = three times a day; TPV = tipranavir; UGT = uridine diphosphate glucuronosyltransferase

**Appendix B, Table 4. Characteristics of Integrase Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 1 of 2)

Generic Name (Abbreviation) Trade Name	Formulations	Dosing Recommendations <sup>a</sup>	Elimination/Metabolic Pathways	Serum Half-Life	Adverse Events <sup>b</sup>
<b>Bictegravir</b> (BIC)  <b>Note:</b> BIC is only available as a component of an FDC.  (BIC/TAF/FTC) <i>Biktarvy</i>	<u>Biktarvy:</u> • (BIC 50 mg plus TAF 25 mg plus FTC 200 mg) tablet	<u>Biktarvy:</u> • 1 tablet once daily	<u>BIC:</u> • CYP3A4 substrate • UGT1A1 mediated glucuronidation	<u>BIC:</u> ~17 hours	<ul style="list-style-type: none"> <li>• Diarrhea</li> <li>• Nausea</li> <li>• Headache</li> </ul>
<b>Dolutegravir</b> (DTG) <i>Tivicay</i>	<u>Tivicay:</u> • 50 mg tablet	<p><u>In ARV-Naive or ARV-Experienced, INSTI-Naive Patients:</u></p> <ul style="list-style-type: none"> <li>• 50 mg once daily</li> </ul> <p><u>In ARV-Naive or ARV-Experienced, INSTI-Naive Patients when Coadministered with EFV, FPV/r, TPV/r, or Rifampin:</u></p> <ul style="list-style-type: none"> <li>• 50 mg BID</li> </ul> <p><u>INSTI-Experienced Patients with Certain INSTI Mutations (See Product Label) or with Clinically Suspected INSTI Resistance:</u></p> <ul style="list-style-type: none"> <li>• 50 mg BID</li> </ul> <p>Take without regard to meals.</p>	<p>UGT1A1 mediated glucuronidation</p> <p>Minor contribution from CYP3A4</p>	~14 hours	<ul style="list-style-type: none"> <li>• Insomnia</li> <li>• Headache</li> <li>• Depression and suicidal ideation (rare; usually in patients with pre-existing psychiatric conditions)</li> <li>• <b>Hepatotoxicity</b></li> <li>• <b>Preliminary data suggest increased rate of neural tube defects in infants born to mothers who were taking DTG at the time of conception.</b></li> <li>• HSRs, including rash, constitutional symptoms, and organ dysfunction (including liver injury) have been reported.</li> </ul>
(DTG/ABC/3TC) <i>Triumeq</i>	<u>Triumeq:</u> • (DTG 50 mg plus ABC 600 mg plus 3TC 300 mg) tablet	<u>Triumeq:</u> • 1 tablet once daily			
(DTG/RPV) <i>Juluca</i>	<u>Juluca:</u> • (DTG 50 mg plus RPV 25 mg) tablet	<u>Juluca:</u> • 1 tablet once daily with a meal			

**Appendix B, Table 4. Characteristics of Integrase Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 2 of 2)

Generic Name (Abbreviation) Trade Name	Formulations	Dosing Recommendations <sup>a</sup>	Elimination/Metabolic Pathways	Serum Half-Life	Adverse Events <sup>b</sup>
<b>Elvitegravir</b> (EVG)  <b>Note:</b> EVG is only available as a component of an FDC.	N/A	N/A	N/A	N/A	<ul style="list-style-type: none"> <li>• Nausea</li> <li>• Diarrhea</li> <li>• Depression and suicidal ideation (rare; usually in patients with pre-existing psychiatric conditions)</li> </ul>
(EVG/c/FTC/TAF) <i>Genvoya</i>	<u>Genvoya:</u> <ul style="list-style-type: none"> <li>• (EVG 150 mg plus COBI 150 mg plus FTC 200 mg plus TAF 10 mg) tablet</li> </ul>	<u>Genvoya:</u> <ul style="list-style-type: none"> <li>• 1 tablet once daily with food</li> </ul> <p><b>Not recommended</b> for patients with CrCl &lt;30 mL/min (see <a href="#">Appendix B, Table 8</a> for the equation for calculating CrCl).</p> <p><b>Not recommended for use with other ARV drugs.</b></p>	EVG: CYP3A, UGT1A1/3 substrate  COBI: CYP3A inhibitor and substrate; CYP2D6 inhibitor	~13 hours (EVG/c)	
(EVG/c/FTC/TDF) <i>Stribild</i>	<u>Stribild:</u> <ul style="list-style-type: none"> <li>• (EVG 150 mg plus COBI 150 mg plus FTC 200 mg plus TDF 300 mg) tablet</li> </ul>	<u>Stribild:</u> <ul style="list-style-type: none"> <li>• 1 tablet once daily with food</li> </ul> <p><b>Not recommended</b> for patients with baseline CrCl &lt;70 mL/min (see <a href="#">Appendix B, Table 8</a> for the equation for calculating CrCl).</p> <p><b>Not recommended for use with other ARV drugs.</b></p>			
<b>Raltegravir</b> (RAL) <i>Isentress</i> <i>Isentress HD</i>	<ul style="list-style-type: none"> <li>• 400 mg tablet</li> <li>• 600 mg tablet (HD)</li> <li>• 25 and 100 mg chewable tablets</li> <li>• 100 mg single packet for oral suspension</li> </ul>	<p><u>In ARV-Naive Patients or ARV-Experienced Patients:</u></p> <ul style="list-style-type: none"> <li>• Isentress: 400 mg BID</li> </ul> <p><u>In ARV-Naive or ARV-Experienced Patients with Virologic Suppression on a Regimen of RAL 400 mg BID:</u></p> <ul style="list-style-type: none"> <li>• Isentress HD: 1200 mg (two 600-mg tablets) once daily</li> </ul> <p><u>With Rifampin:</u></p> <ul style="list-style-type: none"> <li>• Isentress: 800 mg BID</li> <li>• Isentress HD: <b>Not recommended</b></li> </ul> <p>Take without regard to meals.</p>	UGT1A1-mediated glucuronidation	~9 hours	<ul style="list-style-type: none"> <li>• Rash, including Stevens-Johnson syndrome, HSR, and toxic epidermal necrolysis</li> <li>• Nausea</li> <li>• Headache</li> <li>• Diarrhea</li> <li>• Pyrexia</li> <li>• CPK elevation, muscle weakness, and rhabdomyolysis</li> <li>• Insomnia</li> <li>• Depression and suicidal ideation (rare; usually in patients with pre-existing psychiatric conditions)</li> </ul>

<sup>a</sup> For dosage adjustment in patients with hepatic insufficiency, see [Appendix B, Table 8](#).

<sup>b</sup> Also see [Table 15](#).

**Key to Acronyms:** 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; **BIC = bicittegravir**; BID = twice daily; COBI = cobicistat; CPK = creatine phosphokinase; CrCl = creatinine clearance; 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; RAL = raltegravir; **RPV = rilpivirine**; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV/r = tipranavir/ritonavir; UGT = uridine diphosphate gluconyltransferase

**Appendix B, Table 5. Characteristics of the Fusion Inhibitor (Last updated January 29, 2008; last reviewed October 25, 2018)**

Generic Name (Abbreviation) Trade Name	Formulation	Dosing Recommendation	Serum Half-Life	Elimination	Adverse Events <sup>a</sup>
<b>Enfuvirtide</b> (T-20) <i>Fuzeon</i>	<b>Fuzeon:</b> <ul style="list-style-type: none"> <li>Injectable; supplied as lyophilized powder</li> <li>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.</li> <li>Refer to prescribing information for storage instruction.</li> </ul>	<b>Fuzeon:</b> <ul style="list-style-type: none"> <li>90 mg (1 mL) subcutaneously BID</li> </ul>	3.8 hours	Expected to undergo catabolism to its constituent amino acids, with subsequent recycling of the amino acids in the body pool	<ul style="list-style-type: none"> <li>Local injection site reactions (e.g., pain, erythema, induration, nodules and cysts, pruritus, ecchymosis) occur in almost 100% of patients</li> <li>Increased incidence of bacterial pneumonia</li> <li>HSR (&lt;1% of patients). Symptoms may include rash, fever, nausea, vomiting, chills, rigors, hypotension, or elevated serum transaminases. <b>Rechallenge is not recommended.</b></li> </ul>

<sup>a</sup> Also see [Table 15](#).

**Key to Abbreviations:** BID = twice daily; HSR = hypersensitivity reaction; T-20 = enfuvirtide

**Appendix B, Table 6. Characteristics of CCR5 Antagonist (Last updated March 27, 2012; last reviewed October 25, 2018)**

Generic Name (Abbreviation) Trade Name	Formulation	Dosing Recommendations <sup>a</sup>	Serum Half-Life	Elimination/ Metabolic Pathway	Adverse Events <sup>b</sup>
<b>Maraviroc</b> (MVC) <i>Selzentry</i>	<b>Selzentry:</b> <ul style="list-style-type: none"> <li>150 and 300 mg tablets</li> </ul>	<b>Selzentry:</b> <ul style="list-style-type: none"> <li><b>150 mg BID</b> when given with drugs that are strong CYP3A inhibitors (with or without CYP3A inducers), including PIs (except TPV/r)</li> <li><b>300 mg BID</b> when given with NRTIs, T-20, TPV/r, NVP, RAL, and other drugs that are not strong CYP3A inhibitors or inducers</li> <li><b>600 mg BID</b> when given with drugs that are CYP3A inducers, including EFV, ETR, etc. (without a CYP3A inhibitor)</li> </ul> <p>Take without regard to meals.</p>	14–18 hours	CYP3A4 substrate	<ul style="list-style-type: none"> <li>Abdominal pain</li> <li>Cough</li> <li>Dizziness</li> <li>Musculoskeletal symptoms</li> <li>Pyrexia</li> <li>Rash</li> <li>Upper respiratory tract infections</li> <li>Hepatotoxicity, which may be preceded by severe rash or other signs of systemic allergic reactions</li> <li>Orthostatic hypotension, especially in patients with severe renal insufficiency</li> </ul>

<sup>a</sup> For dosage adjustment in hepatic insufficiency, see [Appendix B, Table 8](#).

<sup>b</sup> Also see [Table 15](#).

**Key to Acronyms:** BID = twice daily; CYP = cytochrome P; EFV = efavirenz; ETR = etravirine; MVC = maraviroc; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; RAL = raltegravir; T-20 = enfuvirtide; TPV/r = tipranavir/ritonavir  
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**Appendix B, Table 7. Characteristics of CD4 Post-Attachment Inhibitor (Last updated October 25, 2018; last reviewed October 25, 2018)**

Generic Name (Abbreviation) Trade Name	Formulation	Dosing Recommendations	Serum Half-Life	Elimination/ Metabolic Pathway	Adverse Events
<b>Ibalizumab</b> (IBA) <i>Trogarzo</i>	<u>Trogarzo:</u> <ul style="list-style-type: none"> <li>Single-dose 2 mL vial containing 200 mg/1.33 mL (150 mg/mL) of ibalizumab</li> </ul>	<u>Trogarzo:</u> <ul style="list-style-type: none"> <li>Administer a single loading dose of IBA 2000 mg IV infusion over 30 minutes, followed by a maintenance dose of IBA 800 mg IV infusion over 15 minutes every 2 weeks.</li> <li>See prescribing information for additional instruction in preparation, storage, administration, and monitoring.</li> </ul>	~64 hours	Not well defined.	<ul style="list-style-type: none"> <li>Diarrhea</li> <li>Dizziness</li> <li>Nausea</li> <li>Rash</li> </ul>

**Key to Acronyms:** IBA = ibalizumab; IV = intravenous

**Appendix B, Table 8. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 1 of 7)

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

ARVs Generic Name (Abbreviation) Trade Name	Usual Daily Dose <sup>a</sup>	Dosing in Patients with Renal Insufficiency <sup>b</sup>	Dosing in Patients with Hepatic Impairment	
<b>NRTIs</b>				
Stribild should not be initiated in patients with CrCl <70 mL/min. The following FDCs <b>are not recommended</b> in patients with CrCl <50 mL/min: Atripla, Combivir, Complera, <b>Delstrigo</b> , Epzicom, Triumeq, or Trizivir. <b>Biktarvy</b> , Descovy, Genvoya, Odefsey, <b>Symtuza</b> , and Truvada <b>are not recommended</b> in patients with CrCl <30 mL/min.				
<b>Abacavir</b> (ABC) <i>Ziagen</i>	<ul style="list-style-type: none"> <li>• 300 mg PO BID, <i>or</i></li> <li>• 600 mg PO once daily</li> </ul>	No dose adjustment necessary.	<u>Child-Pugh Class A:</u> <ul style="list-style-type: none"> <li>• 200 mg PO BID (use oral solution)</li> </ul> <u>Child-Pugh Class B or C:</u> <ul style="list-style-type: none"> <li>• <b>Contraindicated</b></li> </ul>	
<b>Didanosine EC</b> (ddl) <i>Videx EC</i>	<u>Body Weight ≥60 kg:</u> <ul style="list-style-type: none"> <li>• 400 mg PO once daily</li> </ul> <u>Body Weight &lt;60 kg:</u> <ul style="list-style-type: none"> <li>• 250 mg PO once daily</li> </ul>	<b>Once-Daily Dose by Body Weight</b>		
		<b>CrCl (mL/min)</b>	<b>≥60 kg</b>	<b>&lt;60 kg</b>
		30–59	200 mg	125 mg
		10–29	125 mg	125 mg
<b>Didanosine Oral Solution</b> (ddl) <i>Videx</i>	<u>Body Weight ≥60 kg:</u> <ul style="list-style-type: none"> <li>• 200 mg PO BID, <i>or</i></li> <li>• 400 mg PO once daily</li> </ul> <u>Body Weight &lt;60 kg:</u> <ul style="list-style-type: none"> <li>• 250 mg PO once daily, <i>or</i></li> <li>• 125 mg PO BID</li> </ul>	<b>Once-Daily Dose by Body Weight</b>		
		<b>CrCl (mL/min)</b>	<b>≥60 kg</b>	<b>&lt;60 kg</b>
		30–59	200 mg	150 mg
		10–29	150 mg	100 mg
<b>Emtricitabine</b> (FTC) <i>Emtriva</i>	<ul style="list-style-type: none"> <li>• 200 mg oral capsule once daily, <i>or</i></li> <li>• 240 mg (24 mL) oral solution once daily</li> </ul>	<b>Dose</b>		
		<b>CrCl (mL/min)</b>	<b>Capsule</b>	<b>Solution</b>
		30–49	200 mg q48h	120 mg q24h
		15–29	200 mg q72h	80 mg q24h
<b>Lamivudine</b> (3TC) <i>Epivir</i>	<ul style="list-style-type: none"> <li>• 300 mg PO once daily, <i>or</i></li> <li>• 150 mg PO BID</li> </ul>	<b>CrCl (mL/min)</b>	<b>Dose</b>	
		30–49	150 mg q24h	
		15–29	1 x 150 mg, then 100 mg q24h	
		5–14	1 x 150 mg, then 50 mg q24h	
<b>Stavudine</b> (d4T) <i>Zerit</i>	<u>Body Weight ≥60 kg:</u> <ul style="list-style-type: none"> <li>• 40 mg PO BID</li> </ul> <u>Body Weight &lt;60 kg:</u> <ul style="list-style-type: none"> <li>• 30 mg PO BID</li> </ul>	<b>Dose</b>		
		<b>CrCl (mL/min)</b>	<b>≥60 kg</b>	<b>&lt;60 kg</b>
		26–50	20 mg q12h	15 mg q12h
		10–25 or on HD <sup>c</sup>	20 mg q24h	15 mg q24h

**Appendix B, Table 8. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 2 of 7)

ARVs Generic Name (Abbreviation) Trade Name	Usual Daily Dose <sup>a</sup>	Dosing in Patients with Renal Insufficiency <sup>b</sup>		Dosing in Patients with Hepatic Impairment
<b>NRTIs, continued</b>				
<b>Tenofovir Alafenamide/ Emtricitabine</b> (TAF/FTC) <i>Descovy</i>	<ul style="list-style-type: none"> <li>TAF for HIV treatment is only available as a component of FDCs (i.e., Descovy, Genvoya, Odefsey, <b>Biktarvy</b>, and <b>Symtuza</b>).</li> <li>TAF 10 mg PO daily with EVG/c (Genvoya) or <b>DRV/c (Symtuza)</b></li> <li>TAF 25 mg PO daily in other FDCs</li> </ul>	<b>CrCl (ml/min)</b>	<b>Dose</b>	<b>Child-Pugh Class A or B:</b> <ul style="list-style-type: none"> <li>No dose adjustment</li> </ul> <b>Child-Pugh Class C:</b> <ul style="list-style-type: none"> <li>No dose recommendation</li> </ul>
		<30 or on HD <sup>c</sup>	Not recommended	
<b>Tenofovir Disoproxil Fumarate</b> (TDF) <i>Viread</i>	• 300 mg PO once daily	<b>CrCl (mL/min)</b>	<b>Dose</b>	No dose adjustment necessary.
		30–49	300 mg q48h	
		10–29	300 mg twice weekly (every 72–96 hours)	
		<10 and not on HD	No recommendation	
		On HD <sup>c</sup>	300 mg q7d	
<b>Tenofovir Disoproxil Fumarate/Emtricitabine</b> (TDF/FTC) <i>Truvada</i>	• 1 tablet PO once daily	<b>CrCl (mL/min)</b>	<b>Dose</b>	No dose recommendation.
		30–49	1 tablet q48h	
		<30 or on HD	Not recommended	
<b>Tenofovir Disoproxil Fumarate/Lamivudine</b> (TDF/3TC) <i>Cimduo</i>	• 1 tablet PO once daily	<b>CrCl (mL/min)</b>	<b>Dose</b>	<b>No dose recommendation.</b>
		<50 or on HD	Not recommended	
<b>Zidovudine</b> (ZDV) <i>Retrovir</i>	• 300 mg PO BID	<b>CrCl (mL/min)</b>	<b>Dose</b>	No dose recommendation.
		<15 or on HD <sup>c</sup>	100 mg TID or 300 mg once daily	
<b>NNRTIs</b>				
<b>Doravirine</b> (DOR) <i>Pifeltro</i>	• 1 tablet PO once daily	No dose adjustment required in mild, moderate, or severe renal impairment. Has not been studied in ESRD or HD.		<b>Child-Pugh Class A or B:</b> <ul style="list-style-type: none"> <li>No dose adjustment</li> </ul> <b>Child-Pugh Class C:</b> <ul style="list-style-type: none"> <li>Not studied</li> </ul>
<b>Doravirine/Tenofovir Disoproxil Fumarate/Lamivudine</b> (DOR/TDF/3TC) <i>Delstrigo</i>	• 1 tablet PO once daily	Not recommended if CrCl <50 mL/min.		<b>Child-Pugh Class A or B:</b> <ul style="list-style-type: none"> <li>No dose adjustment</li> </ul> <b>Child-Pugh Class C:</b> <ul style="list-style-type: none"> <li>Not studied</li> </ul>
<b>Efavirenz</b> (EFV) <i>Sustiva</i>	• 600 mg PO once daily, on an empty stomach, preferably at bedtime	No dose adjustment necessary.		No dose recommendation; use with caution in patients with hepatic impairment.
<b>Efavirenz/Tenofovir Disoproxil Fumarate/Emtricitabine</b> (EFV/TDF/FTC) <i>Atripla</i>	• 1 tablet once daily on an empty stomach, preferably at bedtime	Not recommended if CrCl <50 mL/min. Instead, use the individual drugs and adjust TDF and FTC doses according to CrCl level.		No dose recommendation; use with caution in patients with hepatic impairment.

**Appendix B, Table 8. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 3 of 7)

ARVs Generic Name (Abbreviation) Trade Name	Usual Daily Dose <sup>a</sup>	Dosing in Patients with Renal Insufficiency <sup>b</sup>	Dosing in Patients with Hepatic Impairment
<b>Efavirenz 600 mg/ Tenofovir Disoproxil Fumarate/Lamivudine</b> (EFV/TDF/3TC) <i>Symfi</i>	• 1 tablet once daily on an empty stomach, preferably at bedtime	Not recommended if CrCl <50 mL/min or if patient is on HD. Instead, use the individual drugs and adjust TDF and 3TC doses according to CrCl level.	Not recommended for patients with moderate or severe hepatic impairment. Use caution in patients with mild hepatic impairment.
<b>Efavirenz 400 mg/ Tenofovir Disoproxil Fumarate/Lamivudine</b> (EFV/TDF/3TC) <i>Symfi Lo</i>	• 1 tablet once daily on an empty stomach, preferably at bedtime	Not recommended if CrCl <50 mL/min or if patient is on HD. Instead, use the individual drugs and adjust TDF and 3TC doses according to CrCl level.	Not recommended for patients with moderate or severe hepatic impairment. Use caution in patients with mild hepatic impairment.
<b>Etravirine</b> (ETR) <i>Intence</i>	• 200 mg PO BID	No dose adjustment necessary.	<u>Child-Pugh Class A or B:</u> • No dose adjustment <u>Child-Pugh Class C:</u> • No dose recommendation
<b>Nevirapine</b> (NVP) <i>Viramune</i> or <i>Viramune XR</i>	• 200 mg PO BID, or • 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 200 mg following each dialysis treatment.	<u>Child-Pugh Class A:</u> • No dose adjustment <u>Child-Pugh Class B or C:</u> • <b>Contraindicated</b>
<b>Rilpivirine</b> (RPV) <i>Edurant</i>	• 25 mg PO once daily	No dose adjustment necessary.	<u>Child-Pugh Class A or B:</u> • No dose adjustment <u>Child-Pugh Class C:</u> • No dose recommendation
<b>Rilpivirine/Tenofovir Alafenamide/ Emtricitabine</b> (RPV/TAF/FTC) <i>Odefsey</i>	• 1 tablet PO once daily	Not recommended if CrCl <30 mL/min.	<u>Child-Pugh Class A or B:</u> • No dose adjustment <u>Child-Pugh Class C:</u> • No dose recommendation
<b>Rilpivirine/Tenofovir Disoproxil Fumarate/ Emtricitabine</b> (RPV/TDF/FTC) <i>Complera</i>	• 1 tablet PO once daily	Not recommended if CrCl <50 mL/min. Instead, use the individual drugs and adjust TDF and FTC doses according to CrCl level.	<u>Child-Pugh Class A or B:</u> • No dose adjustment <u>Child-Pugh Class C:</u> • No dose recommendation
<b>Rilpivirine/ Dolutegravir</b> (RPV/DTG) <i>Juluca</i>	• 1 tablet PO once daily with food	No dose adjustment necessary.  In patients with CrCl <30 mL/min, monitor closely for adverse effects.	<u>Child-Pugh Class A or B:</u> • No dose adjustment <u>Child-Pugh Class C:</u> • No dose recommendation
<b>PIs</b>			
<b>Atazanavir</b> (ATV) <i>Reyataz</i>	• 400 mg 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.  <u>In ARV-Naive Patients on HD:</u> • (ATV 300 mg plus RTV 100 mg) once daily  <u>In ARV-Experienced Patients on HD:</u> • ATV or ATV/r not recommended	<u>Child-Pugh Class B:</u> • 300 mg once daily (unboosted) for ARV-naive patients only  <u>Child-Pugh Class C:</u> • Not recommended  RTV boosting is not recommended in patients with hepatic impairment.



**Appendix B, Table 8. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 4 of 7)

ARVs Generic Name (Abbreviation) Trade Name	Usual Daily Dose <sup>a</sup>	Dosing in Patients with Renal Insufficiency <sup>b</sup>	Dosing in Patients with Hepatic Impairment
<b>PIs, continued</b>			
<b>Atazanavir/Cobicistat</b> (ATV/c) <i>Evotaz</i>	• 1 tablet PO once daily	<u>If Used with TDF:</u> • Not recommended if CrCl <70 mL/min	Not recommended in patients with hepatic impairment.
<b>Darunavir</b> (DRV) <i>Prezista</i>	<u>In ARV-Naive Patients and ARV-Experienced Patients with No DRV Resistance Mutations:</u> • (DRV 800 mg plus RTV 100 mg) PO once daily with food  <u>In ARV-Experienced Patients with at Least 1 DRV Resistance Mutation:</u> • (DRV 600 mg plus RTV 100 mg) PO BID	No dose adjustment necessary.	<u>In Patients with Mild-to-Moderate Hepatic Impairment:</u> • No dose adjustment  <u>In Patients with Severe Hepatic Impairment:</u> • Not recommended
<b>Darunavir/Cobicistat</b> (DRV/c) <i>Prezcobix</i>	• 1 tablet PO once daily	<u>If Used with TDF:</u> • Not recommended if CrCl <70 mL/min	<u>Child-Pugh Class A or B:</u> • No dose adjustment  <u>Child-Pugh Class C:</u> • Not recommended
<b>Darunavir/ Cobicistat/Tenofovir Alafenamide/ Emtricitabine</b> (DRV/c/TAF/FTC) <i>Symtuza</i>	• 1 tablet PO once daily	Not recommended if CrCl <30 mL/min.	Not recommended for patients with severe hepatic impairment.
<b>Fosamprenavir</b> (FPV) <i>Lexiva</i>	• 1400 mg PO BID, or • (FPV 1400 mg plus RTV 100–200 mg) PO once daily, or • (FPV 700 mg plus RTV 100 mg) PO BID	No dose adjustment necessary.	<u>In PI-Naive Patients Only</u> <u>Child-Pugh Score 5–9:</u> • 700 mg BID  <u>Child-Pugh Score 10–15:</u> • 350 mg BID  <u>In PI-Naive or PI-Experienced Patients</u> <u>Child-Pugh Score 5–6:</u> • (FPV 700 mg BID plus RTV 100 mg) once daily  <u>Child-Pugh Score 7–9:</u> • (FPV 450 mg BID plus RTV 100 mg) once daily  <u>Child-Pugh Score 10–15:</u> • (FPV 300 mg BID plus RTV 100 mg) once daily

**Appendix B, Table 8. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 5 of 7)

ARVs Generic Name (Abbreviation) Trade Name	Usual Daily Dose <sup>a</sup>	Dosing in Patients with Renal Insufficiency <sup>b</sup>	Dosing in Patients with Hepatic Impairment
<b>PIs, continued</b>			
<b>Indinavir</b> (IDV) <i>Crixivan</i>	• 800 mg PO q8h	No dose adjustment necessary.	<u>In Patients with Mild-to-Moderate Hepatic Insufficiency Due to Cirrhosis:</u> • 600 mg q8h
<b>Lopinavir/Ritonavir</b> (LPV/r) <i>Kaletra</i>	• (LPV 400 mg plus RTV 100 mg) PO BID, or • (LPV 800 mg plus RTV 200 mg) PO once daily	Avoid once-daily dosing in patients on HD.	No dose recommendation; use with caution in patients with hepatic impairment.
<b>Nelfinavir</b> (NFV) <i>Viracept</i>	• 1250 mg PO BID	No dose adjustment necessary.	<u>In Patients with Mild Hepatic Impairment:</u> • No dose adjustment  <u>In Patients with Moderate-to-Severe Hepatic Impairment:</u> • Not recommended
<b>Ritonavir</b> (RTV) <i>Norvir</i>	<u>As a PI-Boosting Agent:</u> • 100–400 mg per day	No dose adjustment necessary.	Refer to recommendations for the primary PI.
<b>Saquinavir</b> (SQV) <i>Invirase</i>	• (SQV 1000 mg plus RTV 100 mg) PO BID	No dose adjustment necessary.	<u>In Patients with Mild-to-Moderate Hepatic Impairment:</u> • Use with caution  <u>In Patients with Severe Hepatic Impairment:</u> • <b>Contraindicated</b>
<b>Tipranavir</b> (TPV) <i>Aptivus</i>	• (TPV 500 mg plus RTV 200 mg) PO BID	No dose adjustment necessary.	<u>Child-Pugh Class A:</u> • Use with caution  <u>Child-Pugh Class B or C:</u> • <b>Contraindicated</b>
<b>INSTIs</b>			
<b>Bictegravir/Tenofovir Alafenamide/ Emtricitabine</b> (BIC/TAF/FTC) <i>Biktarvy</i>	• 1 tablet once daily	Not recommended for use in patients with CrCl <30 mL/min.	<u>Child-Pugh Class C:</u> • Not recommended
<b>Dolutegravir</b> (DTG) <i>Tivicay</i>	• 50 mg once daily, or • 50 mg BID	No dose adjustment necessary.	<u>Child-Pugh Class A or B:</u> • No dose adjustment  <u>Child-Pugh Class C:</u> • Not recommended

**Appendix B, Table 8. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 6 of 7)

ARVs Generic Name (Abbreviation) Trade Name	Usual Daily Dose <sup>a</sup>	Dosing in Patients with Renal Insufficiency <sup>b</sup>	Dosing in Patients with Hepatic Impairment
<b>INSTIs, continued</b>			
<b>Dolutegravir/Abacavir/ Lamivudine</b> (DTG/ABC/3TC) <i>Triumeq</i>	• 1 tablet once daily	Not recommended if CrCl <50 mL/min. Instead, use the individual drugs and adjust 3TC dose according to CrCl.	<u>Child-Pugh Class A:</u> • Patients with mild hepatic impairment require a dose reduction of ABC. Use the individual drugs instead of the fixed-dose combination in these patients.  <u>Child-Pugh Class B or C:</u> • <b>Contraindicated</b> , due to the ABC component
<b>Dolutegravir/ Ralpivirine</b> (DTG/RPV) <i>Juluca</i>	• 1 tablet PO once daily with food	No dose adjustment necessary. In patients with CrCl <30 mL/min, monitor closely for adverse effects.	<u>Child-Pugh Class A or B:</u> • No dose adjustment  <u>Child-Pugh Class C:</u> • No dose recommendation
<b>Elvitegravir/ Cobicistat/Tenofovir Alafenamide/ Emtricitabine</b> (EVG/c/TAF/FTC) <i>Genvoya</i>	• 1 tablet once daily	Not recommended for use in patients with CrCl <30 mL/min.	<u>In Patients with Mild-to-Moderate Hepatic Insufficiency:</u> • No dose adjustment necessary  <u>In Patients with Severe Hepatic Insufficiency:</u> • Not recommended
<b>Elvitegravir/ Cobicistat/Tenofovir Disoproxil Fumarate/ Emtricitabine</b> (EVG/c/TDF/FTC) <i>Stribild</i>	• 1 tablet once daily	EVG/c/TDF/FTC <b>should not be initiated</b> in patients with CrCl <70 mL/min.  Discontinue EVG/c/TDF/FTC if CrCl declines to <50 mL/min while patient is on therapy.	<u>In Patients with Mild-to-Moderate Hepatic Insufficiency:</u> • No dose adjustment necessary  <u>In Patients with Severe Hepatic Insufficiency:</u> • Not recommended
<b>Raltegravir</b> (RAL) <i>Isentress</i> <i>Isentress HD</i>	• 400 mg BID (using Isentress formulation), or • 1200 mg once daily (use Isentress HD formulation only)	No dose adjustment necessary.	<u>In Patients with Mild-to-Moderate Hepatic Insufficiency:</u> • No dose adjustment necessary  <u>In Patients with Severe Hepatic Insufficiency:</u> • No recommendation
<b>Fusion Inhibitor</b>			
<b>Enfuvirtide</b> (T-20) <i>Fuzeon</i>	• 90 mg subcutaneous BID	No dose adjustment necessary.	No dose adjustment necessary.

**Appendix B, Table 8. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency (Last updated October 25, 2018; last reviewed October 25, 2018)** (page 7 of 7)

ARVs Generic Name (Abbreviation) Trade Name	Usual Daily Dose <sup>a</sup>	Dosing in Patients with Renal Insufficiency <sup>b</sup>	Dosing in Patients with Hepatic Impairment
<b>CCR5 Antagonist</b>			
<b>Maraviroc</b> (MVC) <i>Selzentry</i>	<ul style="list-style-type: none"> <li>The recommended dose differs based on concomitant medications and potential for drug-drug interactions. See <a href="#">Appendix B, Table 6</a> for detailed dosing information.</li> </ul>	<p><u>In Patients with CrCl &lt;30 mL/min or Patients Who Are on HD</u></p> <p><i>Without Potent CYP3A Inhibitors or Inducers:</i></p> <ul style="list-style-type: none"> <li>300 mg BID; reduce to 150 mg BID if postural hypotension occurs</li> </ul> <p><i>With Potent CYP3A Inducers or Inhibitors:</i></p> <ul style="list-style-type: none"> <li>Not recommended</li> </ul>	No dose recommendations. MVC concentrations will likely be increased in patients with hepatic impairment.
<b>CD4 Post-Attachment Inhibitor</b>			
<b>Ibalizumab</b> (IBA) <i>Trogarzo</i>	<ul style="list-style-type: none"> <li>Loading dose of 2000 mg IV, followed by a maintenance dose of 800 mg IV every 2 weeks</li> </ul>	No dose adjustment recommended.	No recommendation.

<sup>a</sup> Refer to [Appendix B, Tables 1–7](#) for additional dosing information.

<sup>b</sup> Including patients who are on CAPD and HD.

<sup>c</sup> On dialysis days, take dose after HD session.

**Key to Acronyms:** 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AZT = zidovudine; **BIC = bictegravir**; BID = twice daily; CAPD = chronic ambulatory peritoneal dialysis; COBI = cobicistat; CrCl = creatinine clearance; CYP = cytochrome P; d4T = stavudine; ddi = didanosine; DLV = delavirdine; DRV = darunavir; DRV/c = darunavir/cobicistat; DTG = dolutegravir; **DOR = doravirine**; EC = enteric coated; EFV = efavirenz; ESRD = end stage renal disease; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FDC = fixed-dose combination; FPV = fosamprenavir; FTC = emtricitabine; 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; q(n)d = every (n) days; q(n)h = every (n) hours; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQV = saquinavir; T-20 = enfuvirtide; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TID = three times daily; TPV = tipranavir; XR = extended release; ZDV = zidovudine

Creatinine Clearance Calculation	
Male: $\frac{(140 - \text{age in years}) \times (\text{weight in kg})}{72 \times (\text{serum creatinine})}$	Female: $\frac{(140 - \text{age in years}) \times (\text{weight in kg}) \times (0.85)}{72 \times (\text{serum creatinine})}$

Child-Pugh Score			
Component	Points Scored		
	1	2	3
Encephalopathy <sup>a</sup>	None	Grade 1–2	Grade 3–4
Ascites	None	Mild or controlled by diuretics	Moderate or refractory despite diuretics
Albumin	>3.5 g/dL	2.8–3.5 g/dL	<2.8 g/dL
Total bilirubin <i>or</i>	<2 mg/dL (<34 μmol/L)	2–3 mg/dL (34 μmol/L–50 μmol/L)	>3 mg/dL (>50 μmol/L)
Modified total bilirubin <sup>b</sup>	<4 mg/dL	4–7 mg/dL	>7 mg/dL
Prothrombin time (seconds prolonged) <i>or</i>	<4	4–6	>6
International normalized ratio (INR)	<1.7	1.7–2.3	>2.3

<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

Child-Pugh Classification	Total Child-Pugh Score <sup>a</sup>
Class A	5–6 points
Class B	7–9 points
Class C	>9 points

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