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

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Guidelines Development Process

Table 1. Outline of the Guidelines Development Process

Topic	Comment
Goal of the guidelines	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.
Panel members	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 Panel Roster for a list of current Panel members.
Financial disclosure	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 AIDS*info* website (http://aidsinfo.nih.gov/contentfiles/AA_FinancialDisclosures.pdf).
Users of the guidelines	HIV treatment providers
Developer	Panel on Antiretroviral Guidelines for Adults and Adolescents—a working group of the Office of AIDS Research Advisory Council (OARAC)
Funding source	Office of AIDS Research, NIH
Evidence collection	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 On some occasions, particularly when new information may affect patient safety, unpublished data presented at major conferences or prepared by the FDA and/or manufacturers as warnings to the public may be used as evidence to revise the guidelines.
Recommendation grading	As described in Table 2
Method of synthesizing data	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.
Other guidelines	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.
Update plan	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 AIDS*info* website until the guidelines can be updated with the appropriate changes. Updated guidelines are available on the AIDS*info* website (http://www.aidsinfo.nih.gov).
Public comments	A 2-week public comment period follows release of the updated guidelines on the AIDS*info* 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 contactus@aidsinfo.nih.gov.

Table 2. Rating Scheme for Recommendations

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

Table 3. Laboratory Testing Schedule for Monitoring Patients with HIV Before and After Initiation of Antiretroviral Therapy[a]

Laboratory Test	Timepoint or Frequency of Testing								
	Entry into Care	ART Initiation[b] 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[c]
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 CD4 count <300 cells/mm^3		√ After 2 Years on ART with Consistently Suppressed Viral Load: *CD4 Count 300–500 Cells/mm^3:* • Every 12 months *CD4 Count >500 Cells/mm^3:* • CD4 monitoring is optional	√	√	√ Every 3–6 months
HIV Viral Load	√	√	√[d]	√[e]	√[e]		√	√	Repeat testing is optional
Resistance Testing	√	√[f]					√	√	√[f]
HLA-B*5701 Testing		√ If considering ABC							
Tropism Testing		√ If considering a CCR5 antagonist					√ If considering a CCR5 antagonist or for failure of CCR5 antagonist-based regimen	√	
Hepatitis B Serology (HBsAb, HBsAg, HBcAb total) [g,h,i]	√	√ May repeat if patient is nonimmune and does not have chronic HBV infection[h]				√ May repeat if patient is nonimmune and does not have chronic HBV infection[h]		√ Including prior to starting HCV DAA (see HCV/HIV Infection)	

Laboratory Test	Timepoint or Frequency of Testing								
	Entry into Care	ART Initiation[b] 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[c]
Hepatitis C Screening (HCV antibody or, if indicated, HCV RNA)[j]	√					√ Repeat HCV screening for at-risk patients[k]		√	
Basic Chemistry[l,m]	√	√	√	√				√	√ Every 6–12 months
ALT, AST, T. bilirubin	√	√	√	√				√	√ Every 6–12 months
CBC with Differential	√	√	√ If on ZDV	√ If on ZDV or if CD4 testing is done	√			√	√ Every 3–6 months
Fasting Lipid Profile[n]	√	√			√ 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[m,o]	√	√			√ If on TAF or TDF[l]	√		√	
Pregnancy Test		√ In women of child-bearing potential						√	

[a] 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.[1]

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

[c] 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.

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

[e] 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.

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

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

[h] If HBsAg, HBsAb, and HBcAb are negative, hepatitis B vaccine series should be administered. Refer to HIV Primary Care and Opportunistic Infections guidelines for more detailed recommendations.[1,2]

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

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

[k] 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.

[l] Serum Na, K, HCO_3, Cl, BUN, creatinine, glucose (preferably fasting), and creatinine-based estimated glomerular filtration rate. Serum phosphorus should be monitored in patients with chronic kidney disease who are on TAF- or TDF-containing regimens.[3]

[m] 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.[3] 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).

[n] Consult the National Lipid Association's recommendations for management of patients with dyslipidemia.[4]

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

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; ALT = alanine aminotransferase; ART = antiretroviral therapy; AST = aspartate aminotransferase; BUN = blood urea nitrogen; CBC = complete blood count; CD4 = CD4 T lymphocyte; Cl = chloride; FTC = emtricitabine; HBcAb = hepatitis B core antibody; HBsAb = hepatitis B surface antibody; HBsAg = hepatitis B surface antigen; HBV = hepatitis B virus; HCO3 = 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[a]

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

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

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

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

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

Clinical Setting and Recommendation	Rationale
Drug-Resistance Assay Recommended	
In acute or recent (early) HIV infection: Drug-resistance testing is recommended **(AII)**. A genotypic assay is generally preferred **(AIII)**. Treatment should not be delayed while awaiting results of resistance testing **(AIII)**. If ART is deferred, repeat resistance testing may be considered when therapy is initiated **(CIII)**. A genotypic assay is generally preferred **(AIII)**.	Drug-resistance testing can determine whether drug-resistant virus was transmitted. The initial regimen can be modified once resistance test results are available. Genotypic testing is preferred to phenotypic testing because of lower cost, faster turnaround time, and greater sensitivity for detecting mixtures of wild-type and resistant virus. Repeat testing when ART is initiated may be considered because the patient may have acquired a drug-resistant virus (i.e., superinfection).
In ART-naive patients with chronic HIV infection: Drug-resistance testing is recommended at entry into HIV care to guide selection of initial ART **(AII)**. A genotypic assay is generally preferred **(AIII)**. If an INSTI is considered for an ART-naive patient and transmitted INSTI resistance is a concern, providers should supplement standard resistance testing with a specific INSTI genotypic resistance assay **(BIII)**. If therapy is deferred, repeat resistance testing may be considered before initiation of ART **(CIII)**. A genotypic assay is generally preferred **(AIII)**. If use of a CCR5 antagonist is being considered, a co-receptor tropism assay should be performed **(AI)** (see Co-receptor Tropism Assays).	Transmitted HIV with baseline resistance to at least 1 drug is seen in 10% to 17% of patients, and suboptimal virologic responses may be seen in patients with baseline resistant mutations. Some drug-resistance mutations can remain detectable for years in untreated patients with chronic HIV infection. Genotypic assays provide information on resistance to NRTIs, NNRTIs, PIs, and INSTIs. In some circumstances, INSTI-resistance tests need to be ordered separately (clinicians should check with the testing laboratory). Currently, transmitted INSTI resistance is infrequent, but the risk of a patient acquiring INSTI-resistant strains may be greater in certain known exposure settings. Repeat testing before initiation of ART may be considered because the patient may have acquired a drug-resistant virus (i.e., a superinfection). Genotypic testing is preferred to phenotypic testing because of lower cost, faster turnaround time, and greater sensitivity for detecting mixtures of wild-type and resistant virus.
In patients with virologic failure: Drug-resistance testing is recommended in patients on combination ART with HIV RNA levels >1,000 copies/mL **(AI)**. In patients with HIV RNA levels >500 copies/mL but <1,000 copies/mL, testing may not be successful but should still be considered **(BII)**. A standard genotypic resistance assay is generally preferred for patients experiencing virologic failure on their first or second regimens **(AII)**. When virologic failure occurs while a patient is on an INSTI-based regimen, genotypic testing for INSTI resistance should be performed to determine whether to include drugs from this class in subsequent regimens **(AII)**. If use of a CCR5 antagonist is being considered, a co-receptor tropism assay should be performed **(AI)** (see Co-receptor Tropism Assays). Adding phenotypic testing to genotypic testing is generally preferred in patients with known or suspected complex drug-resistance patterns, particularly to PIs **(BIII)**.	Drug-resistance testing can help determine the role of resistance in drug failure and maximize the clinician's ability to select active drugs for the new regimen. Drug-resistance testing should be performed while the patient is taking prescribed ARV drugs or, if not possible, within 4 weeks after discontinuing therapy **(AII)**. Genotypic testing is preferred to phenotypic testing because of lower cost, faster turnaround time, and greater sensitivity for detecting mixtures of wild-type and resistant HIV. Genotypic assays provide information on resistance to NRTI-, NNRTI-, PI-, and INSTI-associated mutations. In some circumstances, INSTI resistance tests need to be ordered separately (clinicians should check with the testing laboratory). Phenotypic testing can provide additional useful information in patients with complex drug resistance mutation patterns, particularly to PIs.
In patients with suboptimal suppression of viral load: Drug-resistance testing is recommended in patients with suboptimal viral load suppression after initiation of ART **(AII)**.	Testing can determine the role of resistance and thus help the clinician identify the number of active drugs available for a new regimen.

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

Clinical Setting and Recommendation	Rationale
Drug-Resistance Assay Recommended	
In pregnant women with HIV: Genotypic resistance testing is recommended for all pregnant women before initiation of ART **(AIII)** and for those entering pregnancy with detectable HIV RNA levels while on therapy **(AI)**.	The goal of ART in pregnant women with HIV is to achieve maximal viral suppression for treatment of maternal HIV infection and for prevention of perinatal transmission of HIV. Genotypic resistance testing will assist the clinician in selecting the optimal regimen for the patient. However, treatment should not be delayed while awaiting results of resistance testing. The initial regimen can be modified once resistance test results are available.
Drug-Resistance Assay Not Usually Recommended	
After therapy is discontinued: Drug-resistance testing is not usually recommended more than 4 weeks after ARV drugs are discontinued **(BIII)**.	Drug-resistance mutations may become minor species in the absence of selective drug pressure, and available assays may not detect minor drug-resistant species. If testing is performed in this setting, the detection of drug resistance may be of value; however, the absence of resistance does not rule out the presence of minor drug-resistant species.
In patients with low HIV RNA levels: Drug-resistance testing is not usually recommended in patients with a plasma viral load <500 copies/mL **(AIII)**.	Resistance assays cannot be consistently performed given low HIV RNA levels.

Key to Acronyms: ART = antiretroviral therapy; ARV = antiretroviral; INSTI = integrase strand transfer inhibitors; NNRTI = non-nucleoside reverse-transcriptase inhibitors; NRTI = nucleoside reverse-transcriptase inhibitors; PI = protease inhibitor

Table 6. Recommended Antiretroviral Regimens for Initial Therapy

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

Recommended Initial Regimens for Most People with HIV
Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use.
INSTI + 2 NRTIs: • DTG/ABC/3TC[a] **(AI)**—if HLA-B*5701 negative • DTG + tenofovir[b]/FTC[a] (**AI** for both TAF/FTC and TDF/FTC) • EVG/c/tenofovir[b]/FTC (**AI** for both TAF/FTC and TDF/FTC) • RAL[c] + tenofovir[b]/FTC[a] (**AI** for TDF/FTC, **AII** for TAF/FTC)
Recommended Initial Regimens in Certain Clinical Situations
These regimens are effective and tolerable, but have some disadvantages when compared with the regimens listed above, or have less supporting data from randomized clinical trials. However, in certain clinical situations, one of these regimens may be preferred (see Table 7 for examples).
Boosted PI + 2 NRTIs: (In general, boosted DRV is preferred over boosted ATV) • (DRV/c or DRV/r) + tenofovir[b]/FTC[a] (**AI** for DRV/r and AII for DRV/c) • (ATV/c or ATV/r) + tenofovir[b]/FTC[a] **(BI)** • (DRV/c or DRV/r) + ABC/3TC[a] **—if HLA-B*5701–negative (BII)** • (ATV/c or ATV/r) + ABC/3TC[a] **—if HLA-B*5701–negative and HIV RNA <100,000 copies/mL** (**CI** for ATV/r and **CIII** for ATV/c) NNRTI + 2 NRTIs: • EFV + tenofovir[b]/FTC[a] (**BI** for EFV/TDF/FTC and **BII** for EFV + TAF/FTC) • RPV/tenofovir[b]/FTC[a] **(BI)—if HIV RNA <100,000 copies/mL and CD4 >200 cells/mm^3** INSTI + 2 NRTIs: • RAL[c] + ABC/3TC[a] **(CII)—if HLA-B*5701–negative and HIV RNA < 100,000 copies/mL** Regimens to Consider when ABC, TAF, and TDF Cannot be Used:[d] • DRV/r + RAL (BID) **(CI)—if HIV RNA <100,000 copies/mL and CD4 >200 cells/mm^3** • LPV/r + 3TC[a] (BID)[e] **(CI)**

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

[b] 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.

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

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

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

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

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

Table 7. Antiretroviral Regimen Considerations as Initial Therapy based on Specific Clinical Scenarios (page 1 of 4)

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

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
Pre-ART Characteristics	CD4 count <200 cells/mm^3	**Do Not Use the Following Regimens:** • RPV-based regimens • DRV/r + RAL	A higher rate of virologic failure has been observed in those with low pretreatment CD4 count.
	HIV RNA >100,000 copies/mL	**Do Not Use the Following Regimens:** • RPV-based regimens • ABC/3TC with EFV or ATV/r • DRV/r + RAL	Higher rates of virologic failure have been observed in those with high pretreatment HIV RNA.
	HLA-B*5701–positive	**Do not use ABC-containing regimens.**	Abacavir hypersensitivity, a potentially fatal reaction, is highly associated with positivity for the HLA-B*5701 allele.
	ARV must be started before HIV drug resistance results are available (e.g., in a person with acute HIV or when a rapid initiation of ART is warranted). See Initiation of Antiretroviral Therapy.	**Avoid NNRTI-based regimens.** Recommended ART Regimens: • (DRV/r or DRV/c) + tenofovir[a]/FTC; *or* • DTG + tenofovir[a]/FTC	Transmitted mutations conferring NNRTI resistance are more likely than mutations associated with PI or INSTI resistance. Resistance to DRV and DTG emerges slowly; transmitted resistance to DRV is rare and transmitted resistance to DTG has not been reported to date.
ART-Specific Characteristics	A one-pill, once-daily regimen is desired.	STR Options Include: • DTG/ABC/3TC • EFV/TDF/FTC • EVG/c/TAF/FTC • EVG/c/TDF/FTC • RPV/TAF/FTC • RPV/TDF/FTC	Do not use RPV-based regimens if HIV RNA >100,000 copies/mL and CD4 count <200/mm^3. Since RPV-containing STRs are smaller in size than other STRs, they may be considered when a person has difficulty swallowing a larger pill. Do not use DTG/ABC/3TC if patient is HLA-B*5701–positive. See Appendix B, Table 7 for recommendations on ARV dose modification in the setting of renal impairment.
	Food effects	Regimens that Can be Taken Without Regard to Food: • RAL- or DTG-based regimens	Oral bioavailability of these regimens is not significantly affected by food.

Table 7. Antiretroviral Regimen Considerations as Initial Therapy based on Specific Clinical Scenarios (page 2 of 4)

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

Table 7. Antiretroviral Regimen Considerations as Initial Therapy based on Specific Clinical Scenarios
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Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
Presence of Other Conditions, continued	HIV-associated dementia (HAD)	**Avoid EFV-based regimens if possible.** Favor DTG- or DRV-based regimens.	EFV-related neuropsychiatric effects may confound assessment of ART's beneficial effects on improvement of HAD-related symptoms. There is a theoretical CNS penetration advantage of DTG- or DRV-based regimens.
	Narcotic replacement therapy required	**If patient is receiving methadone, consider avoiding EFV-based regimens.** If EFV is used, an increase in methadone dose may be necessary.	EFV reduces methadone concentrations and may lead to withdrawal symptoms.
	High cardiac risk	DTG-, RAL- or RPV-based regimens may be advantageous in this setting. Consider avoiding ABC- and LPV/r -based regimens. If a boosted PI is the desired option, an ATV-based regimen may have advantages over a DRV-based regimen.	An increased CV risk has been observed in some studies. Observational cohort studies reported an association between some PIs (DRV, IDV, FPV, and LPV/r) and an increased risk of CV events, while this has not been seen with ATV (see text); further study is needed.
	Cardiac QTc interval prolongation	Consider avoiding EFV- or RPV-based regimens if taking other medications with known risk of torsades de pointes, or in patients at higher risk of torsades de pointes.	High EFV or RPV concentrations may cause QT prolongation.
	Hyperlipidemia	The Following ARV Drugs Have Been Associated with Dyslipidemia: • PI/r or PI/c • EFV • EVG/c	DTG, RAL, and RPV have fewer lipid effects. TDF has been associated with lower lipid levels than ABC or TAF.
	Patients with history of poor adherence to ARV or inconsistent engagement in care	Consider boosted PI- or DTG-based regimens.	These regimens have a high genetic barrier to resistance.
	Pregnancy	Refer to the Perinatal Guidelines for specific regimen recommendations.	
Presence of Coinfections	HBV infection	Use TDF or TAF, with FTC or 3TC, whenever possible. If TDF and TAF Are Contraindicated: • For treatment of HBV, use FTC or 3TC with entecavir and a suppressive ART regimen (see HBV/HIV Coinfection).	TDF, TAF, FTC, and 3TC are active against both HIV and HBV. 3TC- or FTC-associated HBV mutations can emerge rapidly when these drugs are used without another drug active against HBV.
	HCV treatment required	Refer to recommendations in HCV/HIV Coinfection, with special attention to potential interactions between ARV drugs and HCV drugs.	

Table 7. Antiretroviral Regimen Considerations as Initial Therapy based on Specific Clinical Scenarios (page 4 of 4)

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
Presence of Coinfections, continued	Treating TB disease with rifamycins	TAF is **not recommended** with any rifamycin-containing regimen. If Rifampin is Used: • EFV can be used without dosage adjustment. • If RAL is used, increase RAL dose to 800 mg BID. • Use DTG at 50 mg BID dose only in patients without selected INSTI mutations (refer to product label). If using a PI-based regimen, rifabutin should be used in place of rifampin in the TB regimen.	• Rifamycins may significantly reduce TAF exposure. • Rifampin is a strong inducer of CYP3A4 and UGT1A1 enzymes, causing significant decrease in concentrations of PIs, INSTIs, and RPV. • Rifampin has a less significant effect on EFV concentration than on other NNRTIs, PIs, and INSTIs. • Rifabutin is a less potent inducer and is an option for patients receiving non-EFV-based regimens. Refer to Tables 18a, b, d and e for dosing recommendations for rifamycins used with different ARV agents.

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

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

Table 8. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy (page 1 of 4)

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

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
Dual-NRTI	**ABC/3TC**	• Coformulated with DTG	• May cause life-threatening HSRs in patients positive for the HLA-B*5701 allele. As a result, HLA-B*5701 testing is required before use. • In the ACTG 5202 study, patients with baseline HIV RNA ≥100,000 copies/mL showed inferior virologic responses when ABC/3TC was given with EFV or ATV/r as opposed to TDF/FTC. This difference was not seen when ABC/3TC was used in combination with DTG. • ABC use has been associated with CV disease and cardiac events in some, but not all, observational studies.
	TAF/FTC	• Coformulated with EVG/c or RPV • Active against HBV; a recommended dual-NRTI option for patients with HIV/HBV coinfection • Smaller decline in renal function, less proteinuria, and smaller reductions in BMD than after initiation of TDF/FTC • Approved for patients with eGFR ≥30 mL/min	• TDF is associated with lower lipid levels than TAF, perhaps because TDF results in higher plasma levels of tenofovir, which lowers lipids.
	TDF/FTC	• Coformulated with EFV, EVG/c, and RPV as STRs • Active against HBV; a recommended dual-NRTI option for patients with HIV/HBV coinfection • Better virologic responses than with ABC/3TC in patients with baseline viral load ≥100,000 copies/mL when combined with ATV/r or EFV • Associated with lower lipid levels than ABC or TAF	• Renal toxicity, including proximal tubulopathy and acute or chronic renal insufficiency • Osteomalacia has been reported as a consequence of proximal tubulopathy. • Decreases BMD more than other NRTI combinations
INSTI	**DTG**	• Higher barrier to resistance than EVG or RAL • Coformulated with ABC and 3TC • No food requirement • No CYP3A4 interactions • Favorable lipid profile	• Oral absorption of DTG can be reduced by simultaneous administration with drugs containing polyvalent cations (e.g., Al, Ca, or Mg-containing antacids or supplements, or multivitamin tablets with minerals). See dosing recommendations in Table 18d. • Inhibits renal tubular secretion of Cr and can increase serum Cr without affecting glomerular function • UGT substrate; potential for drug interactions (see Table 18d) • Depression and suicidal ideation (rare; usually in patients with pre-existing psychiatric conditions)

Table 8. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy (page 2 of 4)

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
INSTI, continued	**EVG/c**	• Coformulated with TDF/FTC or TAF/FTC • Compared with ATV/r, causes smaller increases in total and LDL cholesterol	• EVG/c/TDF/FTC is only recommended for patients with baseline CrCl ≥70 mL/min; this regimen should be discontinued if CrCl decreases to <50 mL/min. • COBI is a potent CYP3A4 inhibitor, which can result in significant interactions with CYP3A substrates. • Oral absorption of EVG can be reduced by simultaneous administration with drugs containing polyvalent cations (e.g., Al, Ca, or Mg-containing antacids or supplements, or multivitamin tablets with minerals). See dosing recommendations in Table 18d. • COBI inhibits active tubular secretion of Cr and can increase serum Cr, without affecting renal glomerular function. • Lower genetic barrier to resistance than boosted PI- or DTG-based regimens • Food requirement • Depression and suicidal ideation (rare; usually in patients with pre-existing psychiatric conditions)
	RAL	• Compared to other INSTIs, has longest post-marketing experience • No food requirement • No CYP3A4 interactions • Favorable lipid profile	• Lower genetic barrier to resistance than boosted PI- or DTG-based regimens • Increases in creatine kinase, myopathy, and rhabdomyolysis have been reported. • Rare cases of severe HSRs (including SJS and TEN) have been reported. • Higher pill burden than other INSTI-based regimens • No fixed-dose combination formulation • Oral absorption of RAL can be reduced by simultaneous administration with drugs containing polyvalent cations (e.g., Al, Ca, or Mg-containing antacids or supplements, or multivitamin tablets with minerals). See dosing recommendations in Table 18d. • UGT substrate; potential for drug interactions (see Table 18d) • Depression and suicidal ideation (rare; usually in patients with pre-existing psychiatric conditions)

Table 8. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy (page 3 of 4)

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
NNRTIs	**EFV**	• Coformulated with TDF/FTC • Long-term clinical experience • EFV-based regimens (except for EFV + ABC/3TC) have well-documented efficacy in patients with high HIV RNA.	• Short-and long-term neuropsychiatric (CNS) side effects, including depression and, in some studies, suicidality • Teratogenic in nonhuman primates • Dyslipidemia • Rash • QTc interval prolongation; consider an alternative to EFV in patients taking medications with known risk of causing TdP, or in those at higher risk of TdP. • Transmitted resistance more common than with PIs and INSTIs • Greater risk of resistance at the time of treatment failure than with PIs • Potential for CYP450 drug interactions (see Tables 18b and 19a) • Should be taken on an empty stomach (food increases drug absorption and CNS toxicities)

	RPV	• Coformulated with TDF/FTC and TAF/FTC
		• RPV/TDF/FTC and RPV/TAF/FTC have smaller pill size than other coformulated ARV drugs
		• Compared with EFV:
		  • Fewer CNS adverse effects
		  • Fewer lipid effects
		  • Fewer rashes
			• **Not recommended** in patients with pre-ART HIV RNA >100,000 copies/mL or CD4 count <200 cells/mm^3 because of higher rate of virologic failure in these patients
			• Depression and suicidality
			• QTc interval prolongation; consider an alternative to RPV in patients taking medications with known risk of causing TdP, or in those at higher risk of TdP.
			• Rash
			• Transmitted resistance more common than with PIs and INSTIs
			• More NNRTI-, TDF-, and 3TC-associated mutations at virologic failure than with regimen containing EFV and 2 NRTIs
			• Potential for CYP450 drug interactions (see Tables 18b and 19a)
			• Meal requirement (>390 kcal)
			• Requires acid for adequate absorption
			  • Contraindicated with PPIs
			  • Use with H2 antagonists or antacids with caution (see Table 18a for detailed dosing information).

PIs	**ATV/c** or **ATV/r**	• Higher genetic barrier to resistance than NNRTIs, EVG, and RAL • PI resistance at the time of treatment failure uncommon with PK-enhanced PIs • ATV/c and ATV/r have similar virologic activity and toxicity profiles • Observational cohort studies have found an association between some PIs (DRV, LPV/r, FPV, IDV) and an increased risk of CV events, while this has not been seen with ATV. Further study is needed. See text for discussion.	• Commonly causes indirect hyperbilirubinemia, which may manifest as scleral icterus or jaundice • Food requirement • Absorption depends on food and low gastric pH (see Table 18a for interactions with H2 antagonists, antacids, and PPIs) • Nephrolithiasis, cholelithiasis, nephrotoxicity • GI adverse effects • CYP3A4 inhibitors and substrates: potential for drug interactions (see Table 18a)

Table 8. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy (page 4 of 4)

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
PIs, continued	**ATV/c** (Specific considerations)	• Coformulated tablet	• COBI inhibits active tubular secretion of Cr and can increase serum Cr, without affecting renal glomerular function. • Coadministration with TDF **is not recommended** in patients with CrCl <70 mL/min • Less long-term clinical experience than for ATV/r • COBI (like RTV) is a potent CYP3A4 inhibitor, which can result in significant interactions with CYP3A substrates.
	DRV/c or **DRV/r**	• Higher genetic barrier to resistance than NNRTIs, EVG, and RAL • PI resistance at the time of treatment failure uncommon with PK-enhanced PIs	• Skin rash • Food requirement • GI adverse effects • CYP3A4 inhibitors and substrates: potential for drug interactions (see Table18a) • Increased CV risk in one observational cohort study
	DRV/c (Specific considerations)	• Coformulated tablet	• Less long-term clinical experience than for DRV/r • COBI inhibits active tubular secretion of Cr and can increase serum Cr, without affecting renal glomerular function. • Coadministration with TDF **is not recommended** in patients with CrCl <70 mL/min • Approval primarily based on PK data comparable to that for DRV/r rather than on trials comparing the efficacy of DRV/c and DRV/r • COBI (like RTV) is a potent CYP3A4 inhibitor, which can result in significant interactions with CYP3A substrates.
	LPV/r	• Only RTV-coformulated PI • No food requirement	• Requires 200 mg per day of RTV • Possible higher risk of MI associated with cumulative use of LPV/r • PR and QT interval prolongation have been reported. Use with caution in patients at risk of cardiac conduction abnormalities or in patients receiving other drugs with similar effect. • Possible nephrotoxicity • CYP3A4 inhibitors and substrates: potential for drug interactions (see Table 18a)

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; Al = aluminum; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; BMD = bone mineral density; Ca = calcium; CD4 = CD4 T lymphocyte; CNS = central nervous system; COBI or c = cobicistat; Cr = creatinine; CrCl = creatinine clearance; CV = cardiovascular; CYP = cytochrome P; DRV = darunavir; DTG = dolutegravir; eGFR = estimated glomerular filtration rate; EFV = efavirenz; EVG = elvitegravir; FPV = fosamprenavir; FTC = emtricitabine; GI = gastrointestinal; HBV = hepatitis B virus; HLA = human leukocyte antigen; HSR = hypersensitivity reaction; IDV = indinavir; INSTI = integrase strand transfer inhibitor; LDL = low-density lipoprotein; LPV = lopinavir; Mg = magnesium; MI = myocardial infarction; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PK = pharmacokinetic; PPI = proton pump inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV or r = ritonavir; SJS = Stevens-Johnson syndrome; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TdP = torsades de pointes; TEN = toxic epidermal necrosis; UGT = uridine diphosphate glucuronosyltransferase

Table 9. Antiretroviral Components or Regimens Not Recommended as Initial Therapy page 1 of 2

ARV Components or Regimens	Reasons for Not Recommending as Initial Therapy
NRTIs	
ABC/3TC/ZDV (Coformulated) As triple-NRTI combination regimen	• Inferior virologic efficacy
ABC/3TC/ZDV + TDF As quadruple-NRTI combination regimen	• Inferior virologic efficacy
d4T + 3TC	• Significant toxicities (including lipoatrophy, peripheral neuropathy) and hyperlactatemia (including symptomatic and life-threatening lactic acidosis, hepatic steatosis, and pancreatitis)
ddI + 3TC (or FTC)	• Inferior virologic efficacy • Limited clinical trial experience in ART-naive patients • ddI toxicities such as pancreatitis and peripheral neuropathy
ddI + TDF	• High rate of early virologic failure • Rapid selection of resistance mutations • Potential for immunologic nonresponse/CD4 cell decline • Increased ddI drug exposure and toxicities
ZDV/3TC	• Greater toxicities (including bone marrow suppression, GI toxicities, skeletal muscle myopathy, cardiomyopathy, and mitochondrial toxicities such as lipoatrophy, lactic acidosis, and hepatic steatosis) than recommended NRTIs
NNRTIs	
DLV	• Inferior virologic efficacy • Inconvenient (three times daily) dosing
ETR	• Insufficient data in ART-naive patients
NVP	• Associated with serious and potentially fatal toxicity (hepatic events and severe rash, including SJS and TEN) • When compared to EFV, NVP did not meet noninferiority criteria
PIs	
ATV (Unboosted)	• Less potent than boosted ATV
DRV (Unboosted)	• Use without RTV or COBI has not been studied
FPV (Unboosted) or **FPV/r**	• Virologic failure with unboosted FPV-based regimen may result in selection of mutations that confer resistance to FPV and DRV • Less clinical trial data for FPV/r than for other RTV-boosted PIs
IDV (Unboosted)	• Inconvenient dosing (three times daily with meal restrictions) • Fluid requirement • IDV toxicities such as nephrolithiasis and crystalluria
IDV/r	• Fluid requirement • IDV toxicities such as nephrolithiasis and crystalluria
LPV/r + 2 NRTIs	• Higher pill burden than other PI-based regimens • Higher ritonavir dose than other PI-based regimens • GI intolerance
NFV	• Inferior virologic efficacy • Diarrhea
RTV as sole PI	• High pill burden • GI intolerance • Metabolic toxicity

Table 9. Antiretroviral Components or Regimens Not Recommended as Initial Therapy page 2 of 2

ARV Components or Regimens	Reasons for Not Recommending as Initial Therapy
PIs, continued	
SQV (Unboosted)	• Inadequate bioavailability • Inferior virologic efficacy
SQV/r	• High pill burden • Can cause QT and PR prolongation; requires pretreatment and follow-up ECG
TPV/r	• Inferior virologic efficacy • Higher rate of adverse events than other RTV-boosted PIs • Higher dose of RTV required for boosting than other RTV-boosted PIs
CCR5 Antagonist	
MVC	• Requires testing for CCR5 tropism before initiation of therapy • No virologic benefit when compared with other recommended regimens • Requires twice-daily dosing

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

Table 10. Antiretroviral Options for Patients with Virologic Failure (page 1 of 2)

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

Clinical Scenario	Type of Failing Regimen	Resistance Considerations	New Regimen Options[1,2]	Goal
First Regimen Failure	NNRTI + 2 NRTIs	Most likely resistant to NNRTI +/- 3TC/FTC (i.e., NNRTI mutations +/-M184V/I, without resistance to other NRTIs)[3]	• Boosted PI + 2 NRTIs (at least 1 active) **(AIII)**; or • INSTI + 2 NRTIs (if only 1 of the NRTIs is fully active, or if adherence is a concern, DTG is preferred over EVG or RAL) **(AIII)**; or • Boosted PI + INSTI **(AIII)**	Resuppression
	Boosted PI + 2 NRTIs	Most likely no resistance or resistance only to 3TC/FTC (i.e., M184V/I, without resistance to other NRTIs)[3]	• Continue same regimen **(AII)**; or • Another boosted PI + 2 NRTIs (at least 1 active) **(AII)**; or • INSTI + 2 NRTIs (at least 1 active) (if only 1 of the NRTIs is fully active, or if adherence is a concern, DTG is preferred over EVG or RAL) **(AIII)**; or • Boosted PI + INSTI **(BIII)**	Resuppression
	INSTI + 2 NRTIs	3TC/FTC (i.e., only M184V/I, without resistance to other NRTIs)[3] No INSTI resistance	• Boosted PI + 2 NRTIs (at least 1 active) **(AIII)**; or • DTG + 2 NRTIs (at least 1 active) **(AIII)**; or • Boosted PI + INSTI **(BIII)**	Resuppression
		EVG or RAL +/- 3TC/FTC (i.e., INSTI mutations +/- M184V/I, without resistance to other NRTIs)[3] Resistance to first-line DTG is rare	• Boosted PI + 2 NRTIs (at least 1 active) **(AIII)**; or • DTG[4] twice daily (if sensitive to DTG) + 2 active NRTIs **(AIII)**; or • DTG[4] twice daily (if sensitive to DTG) + a pharmacokinetically boosted PI **(AIII)**	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	• At least 2, and preferably 3, fully active agents **(AI)** • Partially active drugs may be used if no other options are available • Consider using ARV with a different mechanism of action	Resuppression

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

Clinical Scenario	Type of Failing Regimen	Resistance Considerations	New Regimen Options[1,2]	Goal
Second Regimen Failure and Beyond, continued	Multiple or extensive drug resistance with few treatment options	Use past and current genotypic and phenotypic resistance testing to guide therapy Consider viral tropism assay if use of maraviroc is considered Consult an expert in drug resistance, if needed	• Identify as many active or partially active drugs as possible based on resistance testing results • Consider using ARV with a different mechanism of action • Consider enrollment into clinical trials or expanded access programs for investigational agents, if available • Discontinuation of ARVs **is not recommended**	Resuppression, if possible, otherwise, keep viral load as low as possible and CD4 cell count as high as possible
Previously Treated Patients with Suspected Drug Resistance, but Limited or Incomplete ART and Resistance History	Unknown	Obtain medical records if possible Resistance testing may be helpful in identifying prior drug resistance, even if the patient has been off ART, keeping in mind that resistance mutations may not be detected in the absence of drug pressure.	• Consider restarting the old regimen, and obtain viral load and resistance testing 2-4 weeks after reintroduction of therapy • If there is no available ARV history, consider initiating a regimen with drugs with high genetic barrier to resistance (e.g., DTG and/or boosted DRV)	Resuppression

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

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

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

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

Key to Acronyms: 3TC = lamivudine; ART = antiretroviral therapy; ARV = antiretroviral; CD4 = CD4 T lymphocyte; DRV = darunavir; DTG = dolutegravir; EVG = elvitegravir; FTC = emtricitabine; HBV = hepatitis B virus; INSTI = integrase strand transfer inhibitor; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; RAL = raltegravir

Table 11. Identifying, Diagnosing, and Managing Acute and Recent HIV-1 Infection

Suspicion of Acute HIV-1 Infection:

- Acute HIV-1 infection should be considered in individuals with signs or symptoms described below and recent (within 2 to 6 weeks) high risk of exposure to HIV-1.[a]
- Signs, symptoms, or laboratory findings of acute HIV-1 infection may include but are not limited to one or more of the following: fever, lymphadenopathy, skin rash, myalgia, arthralgia, headache, diarrhea, oral ulcers, leucopenia, thrombocytopenia, transaminase elevation.
- High-risk exposures include sexual contact with a person who has HIV-1 infection or a person at risk of HIV-1 infection, sharing of injection drug use paraphernalia, or any exposure in which an individual's mucous membranes or breaks in the skin come in contact with bodily fluid potentially infected with HIV.
- **Differential diagnosis:** The differential diagnosis of HIV-1 infection may include but is not limited to viral illnesses such as Epstein-Barr virus (EBV) and non-EBV (e.g., cytomegalovirus) infectious mononucleosis syndromes, influenza, viral hepatitis, streptococcal infection, or syphilis.

Evaluation/Diagnosis of Acute HIV-1 Infection:

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

Antiretroviral Therapy After Diagnosis of Early HIV-1 Infection:

- ART is recommended for all individuals with HIV **(AI)**, and should be offered to all patients with early HIV-1 infection.
- All pregnant women with early HIV-1 infection should begin ART as soon as possible for their health and to prevent perinatal transmission of HIV-1 **(AI)**.
- A blood sample for genotypic drug resistance testing should be obtained before initiation of ART to guide the selection of the regimen **(AII)**, but the initiation of ART should be done as soon as possible, often prior to availability of resistance test results. If resistance is subsequently identified, treatment should be modified appropriately.
- If no resistance data are available, then a pharmacologically boosted PI-based regimen is recommended because resistance to PIs emerges slowly and clinically significant transmitted resistance to PIs is uncommon. Boosted DRV (DRV/r or DRV/c) plus FTC and either TDF or TAF is a recommended regimen in this setting **(AIII)**. For similar reasons, DTG plus FTC and either TDF or TAF are reasonable options although the data regarding transmission of INSTI-resistant HIV and the efficacy of this regimen in early HIV infection are limited **(AIII)**.
- In patients without transmitted drug-resistant virus, ART should be initiated with one of the combination regimens recommended for patients with chronic HIV-1 infection (see What to Start) **(AIII)**.

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

Key to Acronyms: ART = antiretroviral therapy; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; FTC = emtricitabine; INSTI = integrase strand transfer inhibitor; PI = protease inhibitor; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Table 12. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of HCV in Adults with HIV (page 1 of 4)

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

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

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

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

Selected HIV Drugs	HCV Direct-Acting Antiviral Agents								
	NS5A Inhibitor	NS5B Inhibitor	Coformulated						
				SHOULD NOT BE USED IN THOSE WITH MODERATE TO SEVERE HEPATIC IMPAIRMENT (Cirrhosis classified as Child-Turcotte 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[a]
	Daclatasvir	Sofosbuvir	Ledipasvir/ Sofosbuvir	Sofosbuvir/ Velpatasvir	Sofosbuvir/Velpatasvir/ Voxilaprevir	Glecaprevir/ Pibrentasvir	Elbasvir/ Grazoprevir	Ombitasvir/ Paritaprevir/ Ritonavir plus Dasabuvir[a]	Simeprevir
PIs, continued									
ATV/r or ATV/c	✔ ↓ DCV dose to 30 mg/day	✔	✔ If a PI/r or PI/c is used with TDF, ↑ TDF concentrations are expected. If coadministration is necessary, monitor for TDF-associated toxicities.[d]	✔ If a PI/r or PI/c is used with TDF, ↑ TDF concentrations are expected. If coadministration is necessary, monitor for TDF-associated toxicities.[d]	✘	✘	✘	✔[c]	✘
DRV/r or DRV/c	✔	✔			✔ If a PI/r is used with TDF, ↑TDF concentrations. Monitor for TDF-associated toxicities.[d] Consider monitoring for hepatotoxicity.[e]	✘	✘	✘	✘
LPV/r	✔	✔			✘	✘	✘	✘	✘
TPV/r	?	✘	✘	✘	✘	✘	✘	✘	✘
NNRTIs									
EFV	✔ ↑ DCV dose to 90 mg/day	✔	✔ If used with TDF, monitor for TDF toxicity.	✘	✘	✘	✘	✘	✘
ETR	✔ ↑ DCV dose to 90 mg/day	✔		✘	✘	✘	✘	✘	✘
NVP	✔ ↑ DCV dose to 90 mg/day	✔		✘	✘	?	✘	✘	✘
RPV	✔	✔		✔	✔	✔	✔	✘	✔

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

Selected HIV Drugs	HCV Direct-Acting Antiviral Agents								
	NS5A Inhibitor	NS5B Inhibitor	Coformulated						
				SHOULD NOT BE USED IN THOSE WITH MODERATE TO SEVERE HEPATIC IMPAIRMENT (Cirrhosis classified as Child-Turcotte 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[a]
	Daclatasvir	Sofosbuvir	Ledipasvir/ Sofosbuvir	Sofosbuvir/ Velpatasvir	Sofosbuvir/Velpatasvir/ Voxilaprevir	Glecaprevir/ Pibrentasvir	Elbasvir/ Grazoprevir	Ombitasvir/ Paritaprevir/ Ritonavir plus Dasabuvir[a]	Simeprevir
INSTIs									
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.[e]	✔ If used with TDF, monitor for TDF toxicity. Consider monitoring for hepatotoxicity.[f]	✘	✘	✘
EVG/c/TAF/ FTC	✔ ↓ DCV dose to 30 mg/day	✔	✔	✔	✔ Consider monitoring for hepatotoxicity.[e]	✔ Consider monitoring for hepatotoxicity.[f]	✘	✘	✘
RAL	✔	✔	✔	✔	✔	✔	✔	✔	✔
CCR5 Antagonist									
MVC	✔	✔	✔	✔	✔	✔	?	✘	✔

[a] Dasabuvir must be prescribed with ombitasvir/paritaprevir/ritonavir

[b] Reduce ATV dose to 300 mg and take in the morning at same time as ombitasvir/paritaprevir/ritonavir plus dasabuvir. If RTV cannot be used, choose an alternative HCV regimen.

[c] Take ATV 300 mg in the morning at same time as ombitasvir/paritaprevir/ritonavir plus dasabuvir. If taking RTV or COBI, discontinue RTV or COBI in HIV regimen until HCV therapy is completed.

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

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

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

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

Key to Symbols:

✔ = ARV agents that can be used concomitantly

✘ = ARV agents not recommended

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

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/r = atazanavir/ritonavir; ATV/c = atazanavir/cobicistat; COBI = cobicistat; DAA = direct-acting antiviral agents; DRV = darunavir; DRV/r = darunavir/ritonavir; DRV/c = darunavir/cobicistat; DTG = dolutegravir; DSV = dasabuvir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; HCV = hepatitis C virus; INSTI = integrase strand transfer inhibitor; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PI/c = cobicistat-boosted protease inhibitor; PI/r = ritonavir-boosted protease inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV/r = tipranavir/ritonavir

Table 13. Strategies to Improve Linkage to Care, Retention in Care, Adherence to Appointments, and Adherence to Antiretroviral Therapy (page 1 of 2)

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

Table 13. 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.	• Failure to understand dosing instructions. • Complexity of regimen (e.g., pill burden, size, dosing schedule, food requirements, polypharmacy). • Pill aversion or pill fatigue. • Adverse effects. • Inadequate understanding of drug resistance and its relationship to adherence. • Patient is unaware of appointments or appointments are not scheduled with proper patient input. • Cost-related issues (copays for medications or visits, missed work time). • Depression, drug and alcohol use, homelessness, poverty. • Stigma of taking pills or attending HIV-related appointments. • Nondisclosure of status leading to missed doses, refills, or appointments.
Select from among available effective adherence and retention interventions.	• See https://www.cdc.gov/hiv/research/interventionresearch/compendium/index.html for a summary of best practice interventions to improve linkage, retention, and adherence. • Use adherence-related tools to complement education and counseling interventions (e.g., text messaging, pill box monitors, pill boxes, alarms). • Use community resources to support adherence (e.g., visiting nurses, community workers, family, peer advocates, transportation assistance). • Use patient prescription assistance programs (see above, under "Provide needed resources"). • Use motivational interviews. • Provide outreach for patients who drop out of care • Use peer or paraprofessional treatment navigators. • Recognize positive clinical outcomes resulting from better adherence. • Arrange for DOT in persons in substance use treatment (if feasible). • Enhance clinic support and structures to promote linkage and retention (reminder calls, flexible scheduling, open access, active referrals, and improved patient satisfaction).
Systematically monitor retention in care.	• Record and follow up on missed visits.

Key to Acronyms: ART = antiretroviral therapy; ARTAS = Anti-Retroviral Treatment and Access to Services; ARV = antiretroviral; CD4 = CD4 T lymphocyte; DOT = directly observed therapy; DTG = dolutegravir; PI/r = ritonavir-boosted protease inhibitor; STR = single tablet regimen

Table 14. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy, page 1 of 5

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

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

Table 14. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy, page 2 of 5

Adverse Effect	Drug Class				
	NRTIs	NNRTIs	PIs	INSTIs	EIs
Diabetes Mellitus and Insulin Resistance	**ZDV, d4T, and ddI**	N/A	Reported for some (IDV, LPV/r), but not all, PIs.	N/A	N/A
Dyslipidemia	**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
Gastrointestinal Effects	**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	N/A
Hepatic Effects	**Reported with most NRTIs.** **ZDV, d4T, or ddI:** Steatosis **ddI:** Prolonged exposure linked to noncirrhotic portal hypertension and esophageal varices. **When TAF, TDF, 3TC, and FTC are withdrawn in patients with HBV/HIV coinfection or when HBV resistance develops:** Patients with HBV/HIV coinfection may develop severe hepatic flares.	**EFV:** Fulminant hepatitis progressing to hepatic failure requiring transplantation or death have been reported. **NVP:** Severe hepatotoxicity associated with skin rash or hypersensitivity. Two-week NVP dose escalation may reduce risk. Risk is greater for women with pre-NVP CD4 count >250 cells/mm^3 and men with pre-NVP CD4 count >400 cells/mm^3. NVP should **never** be used for post-exposure prophylaxis. EFV and NVP **are not recommended** in patients with hepatic insufficiency (Child-Pugh class B or C).	**All PIs:** Drug-induced hepatitis and hepatic decompensation have been reported; greatest frequency occurs with TPV/r. **TPV/r: Contraindicated** in patients with hepatic insufficiency (Child Pugh class B or C). **IDV, ATV:** Jaundice due to indirect hyperbilirubinemia.	N/A	**MVC:** Hepatotoxicity with or without rash or HSRs reported.

Table 14. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy, page 3 of 5

Adverse Effect	Drug Class				
	NRTIs	NNRTIs	PIs	INSTIs	EIs
Hypersensitivity Reaction Excluding rash alone or Stevens-Johnson syndrome	**ABC: Contraindicated** if HLA-B*5701-positive. Median onset for HSR is 9 days; 90% of reactions occur within first 6 weeks of treatment. **HSR symptoms (in order of descending frequency):** Fever, rash, malaise, nausea, headache, myalgia, chills, diarrhea, vomiting, abdominal pain, dyspnea, arthralgia, and respiratory symptoms Symptoms worsen with continuation of ABC. Patients should not be rechallenged with ABC if HSR is suspected, regardless of their HLA-B*5701 status.	**NVP:** Hypersensitivity syndrome of hepatotoxicity and rash that may be accompanied by fever, general malaise, fatigue, myalgias, arthralgias, blisters, oral lesions, conjunctivitis, facial edema, eosinophilia, renal dysfunction, granulocytopenia, or lymphadenopathy. Risk is greater for ARV-naive women with pre-NVP CD4 count >250 cells/mm^3 and men with pre-NVP CD4 count >400 cells/mm^3. Overall, risk is higher for women than men. Two-week dose escalation of NVP reduces risk.	N/A	**RAL:** HSR reported when RAL is given with other drugs also known to cause HSR. All ARVs should be stopped if HSR occurs. **DTG:** Reported in <1% of patients in clinical development program.	**MVC:** HSR reported as part of a syndrome related to hepatotoxicity.
Lactic Acidosis	**Reported with NRTIs, especially d4T, ZDV, and ddI:** 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 >10 mmol/L. Women and obese patients at increased risk.	N/A	N/A	N/A	N/A

Table 14. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy, page 4 of 5

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

Table 14. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy, page 5 of 5

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

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

Table 15. Antiretroviral Therapy-Associated Adverse Events That Can Be Managed with Substitution of Alternative Antiretroviral Agent (page 1 of 3)

Adverse Event	ARV Agent(s) or Drug Class		Comments
	Switch from	Switch to	
Bone Density Effects	TDF[a]	ABC[b] or TAF NRTI-sparing regimens or regimens using only 3TC or FTC as the NRTI may be considered, if appropriate.	Declines in BMD have been observed upon initiation of most ART regimens. Switching from TDF to alternative ARV agents has been shown to increase bone density, but the clinical significance of this increase remains uncertain. TAF is associated with smaller declines in BMD than TDF, and patients show improvement in BMD upon switching to TAF. The long-term impact of TAF on patients with osteopenia or osteoporosis is unknown; close clinical monitoring is recommended in this setting.
Bone Marrow Suppression	ZDV	TDF, TAF, or ABC[b]	ZDV has been associated with neutropenia and macrocytic anemia.
Cardiac QTc Interval Prolongation	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.
Cardiovascular Events Myocardial infarction, ischemic stroke	ABC	TDF, TAF, FTC, 3TC	ABC use has been associated with cardiovascular disease and cardiac events in some, but not all, observational studies. TDF has been associated with lower lipid levels than TAF.
	RTV- or COBI-boosted PI regimens, EFV, EVG/c	RAL, DTG, RPV	RAL, DTG, and RPV have less effect on lipids. Large observation cohorts have found an association between some PIs (DRV, FPV, IDV, LPV/r) and an increased risk of CV events. However, this association has not been seen with ATV. Further study is needed.
Central Nervous System, Neuropsychiatric Side Effects Dizziness, suicidal ideation, abnormal dreams, depression	EFV, RPV	ETR or a PI/c or PI/r INSTIs may be considered with monitoring (see Comments column).	In most patients, EFV-related CNS effects subside within 4 weeks after initiation of the drug. Persistent or intolerable effects should prompt substitution of EFV. INSTIs are associated with insomnia. Depression and suicidality have been infrequently reported with INSTI use, primarily in patients with pre-existing psychiatric conditions.
Dyslipidemia Hyper-triglyceridemia (with or without elevated LDL level)	RTV- or COBI-boosted regimens, EFV, EVG/c	RAL, DTG, RPV	Elevated TG and LDL levels are more common with LPV/r and FPV/r than with other RTV-boosted PIs. Improvements in TG and LDL levels have been observed with switch from LPV/r to ATV or ATV/r.[c]

Table 15. 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	
Gastrointestinal Effects Nausea, diarrhea	LPV/r	ATV/c, ATV/r, DRV/c, DRV/r, RAL, DTG, 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 persistent and intolerable.
	Other RTV- or COBI-boosted regimens	RAL, DTG, NNRTIs	In a trial of treatment-naive patients, rates of diarrhea and nausea were similar for EVG/c/TDF/FTC and ATV/r plus TDF/FTC.
Hypersensitivity Reaction	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	
Insulin Resistance	LPV/r, FPV/r	INSTI, RPV	Results of switch studies have been inconsistent. Studies in HIV-negative patients suggest a direct causal effect of LPV/r (and IDV) on insulin resistance. However, traditional risk factors may be stronger risk factors for insulin resistance than use of any PI.
Jaundice and Icterus	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.
Lipoatrophy Subcutaneous fat wasting of limbs, face, buttocks	d4T, ZDV	TDF, TAF, or ABC[b]	Peripheral lipoatrophy is a legacy of 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.
Lipohypertrophy	Accumulation of visceral, truncal, dorso-cervical, and breast fat has been observed during ART, particularly during use of older PI-based regimens (e.g., IDV), but whether ART directly causes fat accumulation remains unclear. There is no clinical evidence that switching to another first line regimen will reverse weight or visceral fat gain.		
Rash	NNRTIs (especially NVP and EFV)	PI- or INSTI-based regimen	Mild rashes developing after initiation of NNRTIs other than NVP rarely require treatment switch. When serious rash develops due to any NNRTI, switch to another drug class.
	DRV/c, DRV/r	ATV/c, ATV/r, or another drug class (e.g., INSTI)	Mild rashes following DRV/r use may resolve with close follow-up only. For more severe reactions, change to an alternative boosted PI or an agent from another drug class.

Table 15. 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	
Renal Effects Including proximal renal tubulopathy and elevated creatinine	TDF[a]	ABC,[b] or 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, RAL, or NNRTI	COBI and DTG, 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.
Stones Nephrolithiasis and cholelithiasis	ATV, ATV/c, ATV/r	DRV/c, DRV/r, INSTI, or NNRTI	Assuming that ATV is believed to be causing the stones.

[a] In patients with chronic active HBV infection, another agent active against HBV should be substituted for TDF.

[b] ABC should be used only in patients known to be HLA-B*5701-negative.

[c] TDF reduces ATV levels; therefore, unboosted ATV should not be coadministered with TDF. Long-term data for unboosted ATV are unavailable.

Key to Abbreviations: ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BMD = bone mineral density; CD4 = CD4 T lymphocyte; CNS = central nervous system; COBI = cobicistat; CrCl = creatine clearance; CV = cardiovascular; d4T = stavudine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; GI = gastrointestinal; HBV = hepatitis B virus; HSR = hypersensitivity reaction; IDV = indinavir; INSTI = integrase strand transfer inhibitor; LDL = low-density lipoprotein; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SCr = serum creatinine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TG = triglycerides; ZDV = zidovudine

Table 16. Monthly Average Wholesale Price[a] of Commonly Used[b] Antiretroviral Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 1 of 3)

ARV Drug (Generic and Brand Names)	Strength, Formulation	Dosing	Tablets, Capsules, or mLs per Month[c]	AWP[a] (Monthly)
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)				
Abacavir				
• Generic	300 mg tablet	2 tablets daily	60 tablets	$502.22–$603.33
• Ziagen	300 mg tablet	2 tablets daily	60 tablets	$670.37
• Ziagen	20 mg/mL solution	30 mL daily	900 mL	$660.86
Emtricitabine				
• Emtriva	200 mg capsules	1 cap daily	30 capsules	$643.82
• Emtriva	10 mg/mL solution	24 mL daily	680 mL (28-day supply)	$608.16
Lamivudine				
• Generic	300 mg tablet	1 tablet daily	30 tablets	$324.33–$429.66
• Epivir	300 mg tablet	1 tablet daily	30 tablets	$498.89
• Epivir	10 mg/mL solution	30 mL daily	900 mL	$498.90
Tenofovir Disoproxil Fumarate				
• Viread	300 mg tablet	1 tablet daily	30 tablets	$1,279.94
Zidovudine				
• Generic	300 mg tablet	1 tablet twice daily	60 tablets	$54.00–$365.44
NRTI Combination Products				
Abacavir/Lamivudine				
• Generic	600/300 mg tablets	1 tablet daily	30 tablets	$1,395.00
• Epzicom	600/300 mg tablets	1 tablet daily	30 tablets	$1,550.05
Tenofovir Alafenamide/Emtricitabine				
• Descovy	25/200 mg tablet	1 tablet daily	30 tablets	$1,881.14
Tenofovir Disoproxil Fumarate/ Emtricitabine				
• Truvada	300/200 mg tablet	1 tablet daily	30 tablets	$1,881.14
Zidovudine/Lamivudine				
• Generic	300/150 mg tablet	1 tablet twice daily	60 tablets	$877.85–$931.61
• Combivir	300/150 mg tablet	1 tablet twice daily	60 tablets	$1,081.70
Abacavir Sulfate/Zidovudine/Lamivudine				
• Generic	300/300/150 mg tablet	1 tablet twice daily	60 tablets	$1,738.46
• Trizivir	300/300/150 mg tablet	1 tablet twice daily	60 tablets	$1,931.64

Table 16. Monthly Average Wholesale Price[a] of Commonly Used[b] Antiretroviral Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 2 of 3)

ARV Drug (Generic and Brand Names)	Strength, Formulation	Dosing	Tablets, Capsules, or mLs per Month[c]	AWP[a] (Monthly)
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)				
Efavirenz • Sustiva	600 mg tablet	1 tablet daily	30 tablets	$1,176.74
Etravirine • Intelence	200 mg tablet	1 tablet twice daily	60 tablets	$1,411.42
Nevirapine • Generic	200 mg tablet	1 tablet twice daily	60 tablets	$648.19–$650.70
• Viramune	200 mg tablet	1 tablet twice daily	60 tablets	$967.63
• Viramune XR	400 mg tablet	1 tablet daily	30 tablets	$897.46
Rilpivirine • Edurant	25 mg tablet	1 tablet daily	30 tablets	$1,160.10
Protease Inhibitors (PIs)				
Atazanavir • Reyataz	200 mg capsule	2 capsules daily	60 capsule	$1,755.91
• Reyataz	300 mg capsule[d]	1 capsule daily	30 capsule	$1,739.50
Atazanavir/Cobicistat • Evotaz	300/150 mg tablet	1 tablet daily	30 tablets	$1,926.56
Darunavir • Prezista	600 mg tablet[e]	1 tablet twice daily	60 tablets	$1,757.77
• Prezista	800 mg tablet[d]	1 tablet daily	30 tablets	$1,757.77
• Prezista	100 mg/mL suspension[e]	8 mL daily 6 mL twice daily	240 mL 360 mL	$1,171.85 $1,757.77
Darunavir/Cobicistat • Prezcobix	800/150 mg tablet	1 tablet daily	30 tabs	$2,009.23
Lopinavir/Ritonavir • Kaletra	200/50 mg tablet	2 tablets twice daily or 4 tablets once daily	120 tablets	$1,160.50
• Kaletra	80/20 mg per mL solution	5 mL twice daily	300 mL	$1,087.97
Tipranavir • Aptivus	250 mg capsule[e]	2 capsules twice daily	120 capsules	$1,786.73
Integrase Strand Transfer Inhibitors (INSTIs)				
Dolutegravir • Tivicay	50 mg tablet	1 tablet once daily	30 tablets	$1,842.82
• Tivicay	50 mg tablet	1 tablet twice daily	60 tablets	$3,685.64
Raltegravir • Isentress	400 mg tablet	1 tablet twice daily	60 tablets	$1,667.52
• Isentress HD	600 mg tablet	2 tablets once daily	60 tablets	$1,667.52
Fusion Inhibitor				
Enfuviritide • Fuzeon	90 mg injection kit	1 injection twice daily	60 doses (1 kit)	$4,302.67
CCR5 Antagonist				
Maraviroc • Selzentry	150 mg tablet	1 tablet twice daily	60 tablets	$1,679.68
• Selzentry	300 mg tablet	1 tablet twice daily	60 tablets	$1,679.68
• Selzentry	300 mg tablet	2 tablets twice daily	120 tablets	$3,359.36

Table 16. Monthly Average Wholesale Price[a] of Commonly Used[b] Antiretroviral Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 3 of 3)

ARV Drug (Generic and Brand Names)	Strength, Formulation	Dosing	Tablets, Capsules, or mLs per Month[c]	AWP[a] (Monthly)
Coformulated Combination Products as Single Tablet Regimens				
Dolutegravir/Abacavir/Lamivudine • Triumeq	50/600/300 mg tablet	1 tablet daily	30 tablets	$3,118.62
Efavirenz/Tenofovir Disoproxil Fumarate/Emtricitabine • Atripla	600/300/200 mg tablet	1 tablet daily	30 tablets	$3,057.89
Elvitegravir/Cobicistat/Tenofovir Alafenamide/Emtricitabine • Genvoya	150/150/10/200 mg tablet	1 tablet daily	30 tablets	$3,306.92
Elvitegravir/Cobicistat/Tenofovir Disoproxil Fumarate/Emtricitabine • Stribild	150/150/300/200 mg tablet	1 tablet daily	30 tablets	$3,707.99
Rilpivirine/Tenofovir Alafenamide/ Emtricitabine • Odefsey	25/25/200 mg tablet	1 tablet daily	30 tablets	$3,009.29
Rilpivirine/Tenofovir Disoproxil Fumarate/Emtricitabine • Complera	25/300/200 mg tablet	1 tablet daily	30 tablets	$3,216.92
Pharmacokinetic Enhancers (Boosters)				
Cobicistat • Tybost	150 mg tablet	1 tablet daily	30 tablets	$246.84
Ritonavir: Total daily dose depends on the dose of the concomitant PI (100 mg once or twice daily, or 200 mg twice daily)				
• Norvir	100 mg tablet	1 tablet once daily	30 tablets	$308.60
• Norvir	80 mg/mL solution	100 mg daily	37.5 mL (of a 240 mL bottle)	$270.04

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

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

[c] Represents 30 days or as specified.

[d] Should be used in combination with ritonavir or cobicistat. Please refer to Appendix B, Table 3 for ritonavir doses.

[e] Should be used in combination with ritonavir. Please refer to Appendix B, Table 3 for ritonavir doses.

Key to Acronyms: ARV = antiretroviral; XR = extended release

Table 17. Mechanisms of Antiretroviral-Associated Drug Interactions (page 1 of 2)

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

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

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	
INSTIs								
DTG	...	Concentration decreased by products containing polyvalent cations (e.g., Ca, Mg, Al, Fe, Zn)	Substrate	3A4 (minor)	...	...	Substrate	Inhibitor of renal transporters OCT2 and MATE
EVG	...		...	3A4	...	2C9	Substrate	...
RAL	...		...	...	...	...	Substrate	...
PK Enhancers (Boosters)								
COBI	...	...	Inhibitor	3A4	3A4, 2D6	...	...	...
RTV	...	...	Substrate, inhibitor	3A4, 2D6	3A4, 2D6	1A2, 2B6, 2C8, 2C9, 2C19	Inducer	...
PIs **Note:** When PIs are coadministered with PK enhancers (boosters), the pharmacologic properties of both agents should be considered when assessing potential drug interactions.								
ATV	Concentration decreased	...	Substrate, inducer, inhibitor	3A4	3A4, 2C8 (weak)	...	Inhibitor	OATP inhibitor

Table 17. Mechanisms of Antiretroviral-Associated Drug Interactions (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	
PIs, continued								
DRV	...	...	Substrate	3A4	3A4	2C9	...	OATP inhibitor
FPV	Concentration decreased by H2 antagonist	...	Substrate, inhibitor	3A4	3A4	3A4 (weak)	...	...
LPV	...	...	Substrate	3A4	3A4	...	...	OATP inhibitor
SQV	...	...	Substrate, inhibitor	3A4	3A4	...	...	OATP inhibitor
TPV	...	...	Substrate, inducer	3A4	2D6	3A4, 1A2, 2C19	...	OATP inhibitor
NNRTIs								
EFV	...	...	...	2B6 (primary), 2A6, 3A4	2C9, 2C19, 3A4	3A4, 2B6	...	...
ETR	...	...	Inhibitor	3A4, 2C9, 2C19	2C9, 2C19	3A4	...	...
NVP	...	...	...	3A4, 2B6	...	3A4, 2B6	...	...
RPV	Concentration decreased	...	...	3A4	...	...	...	...
NRTIs								
ABC	...	...	...	...	...	...	Substrate	Alcohol dehydrogenase substrate
FTC	...	...	...	...	...	...	...	...
3TC	...	...	...	...	...	...	...	...
TAF	...	...	Substrate	...	...	...	...	OATP substrate
TDF	...	...	Substrate	...	...	...	...	Competition of active renal tubular secretion
ZDV	...	...	...	...	...	...	...	Glucuronidation
CCR5 Antagonist								
MVC	...	...	Substrate	3A4	...	...	...	...
Fusion Inhibitor								
T20	...	...	...	...	...	...	...	...

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; Al = aluminum; ARV = antiretroviral; ATV = atazanavir; Ca = calcium; COBI = cobicistat; CYP = cytochrome P; DRV = darunavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; Fe = iron; FPV = fosamprenavir; FTC = emtricitabine; INSTI = integrase strand transfer inhibitor; LPV = lopinavir; MATE = multidrug and toxin extrusion transporter; Mg = magnesium; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitors; NRTI = nucleoside reverse transcriptase inhibitors; NVP = nevirapine; OCT2 = organic cation transporter 2; OATP = organic anion-transporting polypeptide; PK = pharmacokinetic; PI = protease inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQV = saquinavir; T20 = enfuvirtide; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV = tipranavir; UGT = uridine diphosphate glucuronosyltransferase; ZDV = zidovudine; Zn = zinc

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

This table provides known or predicted information regarding PK interactions between PIs and non-ARV drugs. When information is available, interactions for specific PK-boosted (with either RTV or COBI) and unboosted ATV are listed separately. The term "All PIs" refers to both unboosted ATV and PIs boosted with either RTV or COBI, except the PIs noted below. For interactions between ARV agents and for dosing recommendations, refer to Tables 18c, 19a, and 19b.

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

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

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers			
Antacids	ATV, ATV/c, ATV/r	When given simultaneously, ↓ ATV expected	Give ATV at least 2 hours before or 1 to 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-naive patients. Unboosted ATV + 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-naive patients or 20 mg BID in ART-experienced patients. Give ATV 300 mg + 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 + COBI 150 mg or RTV 100 mg.
	DRV/c, DRV/r, LPV/r	↔ demonstrated or expected	No dose adjustment necessary.
PPIs	ATV (unboosted)	↓ ATV	**PPIs are not recommended in patients receiving unboosted ATV.** 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-naive patients. PPIs should be administered at least 12 hours before ATV/c or ATV/r. **PPIs are not recommended in PI-experienced patients.**
	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 omeprazole dose to no more than 40 mg daily if needed.

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

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers, continued			
PPIs, continued	TPV/r	Omeprazole AUC ↓ 70%	**Coadministration is not recommended.** If coadministration is necessary, dose increases of omeprazole may be considered based on clinical response.
Anticoagulants and Antiplatelets			
Apixaban	PI/c, PI/r	↑ apixaban expected	**Coadministration is not recommended.** Consider alternative ARV or warfarin. If coadministration is necessary, reduce apixaban dose by 50% and monitor for apixaban toxicity.
Betrixaban	PI/r	↑ or ↓ betrixaban possible	**Coadministration is not recommended.** Consider alternative ARV or warfarin.
	ATV/c, DRV/c	↑ betrixaban expected	**Coadministration is not recommended.** Consider alternative ARV or warfarin.
Dabigatran	PI/r	With RTV 100 mg + dabigatran taken simultaneously: ↔ dabigatran Dabigatran given 2 hours before RTV 100 mg: dabigatran AUC ↓ 29%	The extent of interaction of PI/r + dabigratran is unknown. Consider alternative ARV or warfarin. If coadministered, take dabigatran and PI/r simultaneously.
	ATV/c, DRV/c	With COBI 150 mg: dabigatran AUC ↑ 110%–127%	**Coadministration is not recommended.** Consider alternative ARV or warfarin.
Edoxaban	PI/r	↑ or ↓ edoxaban possible	**Coadministration is not recommended.** Consider alternative ARV or warfarin.
	ATV/c, DRV/c	↑ edoxaban expected	**Coadministration is not recommended.** Consider alternative ARV or warfarin.
Rivaroxaban	PI/c, PI/r	↑ rivaroxaban expected	**Coadministration is not recommended.** Consider alternative ARV or warfarin.
Ticagrelor	All PIs	↑ ticagrelor expected	**Coadministration is not recommended.** Consider alternative ARV or warfarin.
Vorapaxar	All PIs	↑ vorapaxar expected	**Coadministration is not recommended.** Consider alternative ARV or warfarin.
Warfarin	PI/r	↓ warfarin possible	Monitor INR closely when stopping or starting PI/r and adjust warfarin dose accordingly.
	ATV/c, DRV/c	No data	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.
Anticonvulsants			
Carbamazepine	ATV (unboosted)	May ↓ PI levels substantially	**Do not coadminister.** Consider alternative anticonvulsant or ARV.
	ATV/c, DRV/c	↓ cobicistat expected ↓ PI levels expected	**Contraindicated.**
	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. **Do not coadminister with LPV/r once daily.**

Table 18a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 3 of 17)

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Anticonvulsants, continued			
Carbamazepine, continued	DRV/r	Carbamazepine AUC ↑ 45% DRV: no significant change	Monitor anticonvulsant level and adjust dose accordingly.
Oxcarbazepine, Eslicarbazepine	All PIs	↓ PI possible	Consider alternative anticonvulsant or ARV. If coadministration is necessary, monitor for virologic response. Consider monitoring anticonvulsant and PI concentration.
Ethosuximide	All PIs	↑ ethosuximide possible	Clinically monitor for ethosuxamide toxicities.
Lamotrigine	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	
	ATV/c, DRV/c	No data	Monitor lamotrigine concentration or consider alternative anticonvulsant.
Phenobarbital	ATV/c, DRV/c	↓ cobicistat expected ↓ PI levels expected	**Contraindicated.**
	ATV (unboosted), PI/r	May ↓ PI levels substantially	Consider alternative anticonvulsant or monitor levels of both drugs and assess virologic response. **Do not coadminister with LPV/r once daily or unboosted ATV.**
Phenytoin	ATV (unboosted)	May ↓ PI levels substantially	**Do not coadminister.** 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.
	ATV/c, DRV/c	↓ cobicistat expected ↓ PI levels expected	**Contraindicated.**
	LPV/r	Phenytoin AUC ↓ 31% LPV/r AUC ↓ 33%	Consider alternative anticonvulsant or monitor levels of both drugs and assess virologic response. **Do not coadminister with LPV/r once daily.**
Valproic Acid	PI/c, PI/r	↓ or ↔VPA possible LPV AUC ↑ 75%	Monitor VPA levels and virologic response. Monitor for LPV-related toxicities.
Antidepressants, Anxiolytics, and Antipsychotics (also see Sedative/Hypnotics section below)			
Bupropion	LPV/r	Bupropion AUC ↓ 57%	Titrate bupropion dose based on clinical response.
	TPV/r	Bupropion AUC ↓ 46%	
Buspirone	All PIs	↑ buspirone expected	Use a low dose of buspirone with caution and titrate buspirone dose based on clinical response.
Fluvoxamine	All PIs	↑ or ↓ PI possible	Consider alternative therapeutic agent.
Lurasidone	PI/c, PI/r	↑ lurasidone expected	**Contraindicated.**
	ATV (unboosted)	↑ lurasidone expected	Consider alternative therapy. If coadministration is necessary, reduce lurasidone dose by 50%.

Table 18a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 4 of 17)

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antidepressants, Anxiolytics, and Antipsychotics (also see Sedative/Hypnotics section below), continued			
Other Selective Serotonin Reuptake Inhibitors (SSRIs) (e.g., citalopram, escitalopram, fluoxetine, paroxetine, sertraline)	RTV	Escitalopram ↔	Titrate SSRI dose based on clinical response.
	DRV/r	Paroxetine AUC ↓ 39% Sertraline AUC ↓ 49%	
	ATV/r, LPV/r, TPV/r	No data	
	ATV/c, DRV/c	Effects unknown	Titrate SSRI dose using the lowest available initial or maintenance dose.
Pimozide	All PIs	↑ pimozide expected	**Contraindicated.**
Quetiapine	All PIs	↑ quetiapine expected	Starting Quetiapine in a Patient Receiving a PI: Start quetiapine at the lowest dose and titrate up as needed. Monitor for quetiapine effectiveness and adverse effects. Starting a PI in a Patient Receiving a Stable Dose of Quetiapine: Reduce quetiapine dose to 1/6 of the original dose. Closely monitor for quetiapine effectiveness and adverse effects.
Other Antipsychotics (e.g., perphenazine, risperidone, thioridazine)	PI/c, PI/r	↑ antipsychotic possible	Titrate antipsychotic dose using the lowest initial dose, or adjust maintenance dose accordingly. Monitor for toxicities.
Trazodone	All PIs	RTV 200 mg BID (for 2 days) ↑ trazodone AUC 240%	Use lowest dose of trazodone and monitor for CNS and CV adverse effects.
Tricyclic Antidepressants Amitriptyline, desipramine, doxepin, imipramine, nortriptyline	All PIs	↑ TCA expected	Use lowest possible TCA dose and titrate based on clinical assessment and/or drug levels.
Antifungals			
Fluconazole	PI/c, ATV/r, DRV/r, LPV/r	No significant effect observed or expected	No dose adjustment necessary.
	TPV/r	TPV AUC ↑ 50%	Fluconazole >200 mg daily is not recommended. If high-dose fluconazole is indicated, consider alternative ARV.
Isavuconazole	LPV/r	Isavuconazole AUC ↑ 96% 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.
Itraconazole	All PIs	↑ itraconazole possible ↑ PI possible	Consider monitoring itraconazole level to guide dosage adjustments. Doses >200 mg/day are not recommended with PI/r, ATV/c, or DRV/c unless dosing is guided by itraconazole levels.

Table 18a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 5 of 17)

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antifungals, continued			
Posaconazole	ATV/r	ATV AUC ↑ 146% ↑ posaconazole possible	If coadministered, monitor for PI adverse effects. Consider monitoring posaconazole concentrations and toxicities.
	ATV	ATV AUC ↑ 268% ↑ posaconazole possible	
	ATV/c, DRV/c, DRV/r, LPV/r, TPV/r	↑ PI possible ↑ posaconazole possible	
Voriconazole	ATV (unboosted)	↑ voriconazole possible ↑ PI possible	Monitor for toxicities.
	All PI/r	RTV 400 mg BID ↓ voriconazole AUC 82% RTV 100 mg BID ↓ voriconazole AUC 39%	**Do not coadminister voriconazole and RTV or COBI unless benefit outweighs risk.** If coadministered, consider monitoring voriconazole concentration and adjust dose accordingly.
	ATV/c, DRV/c	Effects unknown	
Antihyperglycemics			
Canagliflozin	PI/r	↓ canagliflozin expected	If a patient is already tolerating canagliflozin 100 mg daily, has an eGFR >60 mL/min/1.73m^2, and requires additional glycemic control, consider increasing canagliflozin dose to 300 mg daily.
	PI/c	↓ canagliflozin possible	If used in combination, monitor glycemic control.
Saxagliptin	All PIs	↑ saxagliptin expected	Limit saxagliptin dose to 2.5 mg once daily
Dapagliflozin/ Saxagliptin	All PIs	↑ saxagliptin expected	**Do not coadminister**, as this coformulated drug contains 5 mg of saxagliptin.
Antimalarials			
Artemether/ Lumefantrine	DRV/r	Artemether AUC ↓ 16% DHA[a] AUC ↓ 18% Lumefantrine AUC ↑ 2.5-fold	Clinical significance unknown. If used, monitor closely for antimalarial efficacy and lumefantrine toxicity.
	DRV/c	↑ lumefantrine expected Effect on artemether unknown	
	LPV/r	Artemether AUC ↓ 40% DHA AUC ↓ 17% Lumefantrine AUC ↑ 470%	
Artesunate/ Mefloquine	LPV/r	Dihydroartemisinin AUC ↓ 49% Mefloquine AUC ↓ 28% LPV ↔	Clinical significance unknown. If used, monitor closely for antimalarial efficacy.

Table 18a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 6 of 17)

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

Table 18a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 7 of 17)

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antimycobacterials (for treatment of *Mycobacterium tuberculosis* and nontuberculosis mycobacterial infections), continued			
Rifabutin, continued	TPV/r	Rifabutin and metabolite AUC ↑ 333%	
Rifampin	All PIs	↓ PI concentration by >75%	**Contraindicated.** Additional RTV does not overcome this interaction and may increase hepatotoxicity. Additional COBI is not recommended. Consider rifabutin if a rifamycin is indicated.
Rifapentine	All PIs	↓ PI expected	**Do not coadminister.**
Antipneumocystis and Antitoxoplasmosis Drug			
Atovaquone	ATV/r	Atovaquone ↔	No dose adjustment necessary.
Cardiac Medications			
Amiodarone	TPV/r	↑ both amiodarone and PI possible	**Contraindicated.**
	All PIs except TPV/r	↑ both amiodarone and PI possible	Use with caution. Monitor for amiodarone toxicity and consider ECG and amiodarone drug level monitoring.
Antiarrhythmics (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	**Do not coadminister.** Consider alternative antiarrhythmics or ARV.
Dronedarone	ATV (unboosted)	↑ dronedarone possible	**Do not coadminister.**
	PI/c, PI/r	↑ dronedarone expected	**Contraindicated.**
Flecanide	All PIs except TPV/r	↑ flecainide possible	**Do not coadminister.**
	TPV/r	↑ flecanide expected	**Contraindicated.**
Propafenone	All PIs except TPV/r	↑ propafenone possible	**Do not coadminister.**
	TPV/r	↑ propafenone expected	**Contraindicated.**
Quinidine	All PIs except TPV/r	↑ quinidine possible	**Do not coadminister.**
	TPV/r	↑ quinidine expected	**Contraindicated.**
Beta-Blockers (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).

Table 18a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 8 of 17)

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Cardiac Medications, continued			
Bosentan	All PIs	LPV/r ↑ bosentan 48-fold (day 4) and 5-fold (day 10) ↓ ATV expected	**Do not coadminister bosentan and unboosted ATV.** In Patients on a PI (Other than Unboosted ATV) >10 Days: • Start bosentan at 62.5 mg once daily or every other day. In Patients on Bosentan who Require a PI (Other than Unboosted ATV): • Stop bosentan ≥36 hours before PI initiation and restart bosentan 10 days after PI initiation at 62.5 mg once daily or every other day. When Switching Between COBI and RTV: • Maintain same bosentan dose.
Calcium Channel Blockers (CCBs), Except Diltiazem	All PIs	↑ dihydropyridine possible ↑ verapamil possible	Use with caution. Titrate CCB dose and monitor closely. ECG monitoring is recommended when CCB is used with ATV.
Digoxin	PI/r, PI/c	RTV (200 mg BID) ↑ digoxin AUC 29% and ↑ half-life 43% DRV/r ↑ digoxin AUC 36% COBI ↑ digoxin C_{max} 41%, AUC ↔	Use with caution. Monitor digoxin levels. Digoxin dose may need to be decreased. Titrate initial digoxin dose.
Diltiazem	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.
Eplerenone	PI/c, PI/r	↑ eplerenone expected	**Contraindicated.**
Ranolazine	ATV (unboosted)	↑ ranolazine possible	**Do not coadminister.**
	PI/c, PI/r	↑ ranolazine expected	**Contraindicated.**
Ivabradine	All PIs	↑ ivabradine expected	**Contraindicated.**
Corticosteroids			
Beclomethasone 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.
Budesonide, Ciclesonide, Fluticasone, Mometasone 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. **Do not coadminister unless potential benefits of inhaled or intranasal corticosteroid outweigh the risks of systemic corticosteroid adverse effects.** Consider an alternative corticosteroid (e.g., beclomethasone).

Table 18a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 9 of 17)

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Corticosteroids, continued			
Betamethasone, Budesonide Systemic	All PIs	↑ glucocorticoids possible ↓ PI possible	Coadministration can result in adrenal insufficiency and Cushing's syndrome. **Do not coadminister unless potential benefits of systemic corticosteroid outweigh the risks of systemic corticosteroid adverse effects.**
Dexamethasone Systemic	All PIs	↑ glucocorticoids possible ↓ PI possible	Consider alternative corticosteroid for long-term use. If coadministration is necessary, monitor virologic response to ART.
Prednisone, Prednisolone Systemic	LPV/r	↑ prednisolone AUC 31%	Coadministration may be considered if the potential benefits outweigh the risks of systemic corticosteroid adverse effects. If coadministered, monitor for adrenal insufficiency, Cushing's syndrome, and other corticosteroid-associated toxicities.
	All PIs	↑ prednisolone possible	
Betamethasone, Methylpred-nisolone, Triamcinolone Local injections, including intra-articular, epidural, or intra-orbital	All PIs	↑ glucocorticoids expected	**Do not coadminister.** Coadministration can result in adrenal insufficiency and Cushing's syndrome.
Hepatitis C Direct-Acting Antiviral Agents			
Daclatasvir	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.
Dasabuvir + Paritaprevir/ Ombitasvir/RTV	ATV (unboosted)	ATV ↔	ATV 300 mg alone, **without COBI or additional RTV**, should be given in the morning with dasabuvir + paritaprevir/ombitasvir/RTV.
	DRV	DRV C_{min} ↓ 43% to 48%	**Do not coadminister.**
	LPV/r	Paritaprevir AUC ↑ 117%	**Do not coadminister.**
	ATV/c, DRV/c, TPV/r	No data	**Do not coadminister.**

Table 18a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 10 of 17)

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hepatitis C Direct-Acting Antiviral Agents, continued			
Elbasvir/ Grazoprevir	ATV/r	Elbasvir AUC ↑ 4.8-fold Grazoprevir AUC ↑ 10.6-fold ATV ↔ by elbasvir ATV AUC ↑ 43% by grazoprevir	**Contraindicated.** May increase the risk of ALT elevations due to a significant increase in grazoprevir plasma concentrations caused by OATP1B1/3 inhibition.
	DRV/r	Elbasvir AUC ↑ 66% Grazoprevir AUC ↑ 7.5-fold DRV ↔	
	LPV/r	Elbasvir AUC ↑ 3.7-fold Grazoprevir AUC ↑ 12.9-fold LPV ↔	
	ATV (unboosted), ATV/c, DRV/c, TPV/r	↑ grazoprevir expected	
Glecaprevir/ Pibrentasvir	ATV (unboosted), ATV/c, ATV/r	When Given with ATV/r 300/100 mg Once Daily: • Glecaprevir AUC ↑ 6.5-fold • Pibrentasvir AUC ↑ 64%	**Contraindicated.**
	DRV/c, DRV/r	When Given with DRV/r 800/100 mg Once Daily: • Glecaprevir AUC ↑ 5-fold • ↔ pibrentasvir	**Do not coadminister.**
	LPV/r	↑ glecaprevir AUC 4-fold ↑ pibrentasvir 2.5-fold	**Do not coadminister.**
	TPV/r	↑ glecaprevir and pibrentasvir expected	**Do not coadminister.**
Ledipasvir/ Sofosbuvir	ATV/r	ATV AUC ↑ 33% Ledipasvir AUC ↑ 113% ↔ sofosbuvir	No dose adjustment 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	**Do not coadminister.**

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

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hepatitis C Direct-Acting Antiviral Agents, continued			
Simeprevir	All PIs	Compared with Simeprevir 150 mg Alone, Simeprevir 50 mg + DRV/r 800/100 mg Daily: • Simeprevir AUC ↑ 159% RTV 100 mg BID ↑ simeprevir AUC 618%	**Do not coadminister.**
Sofosbuvir	TPV/r	↓ sofosbuvir expected	**Do not coadminister.**
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	**Do not coadminister.**
Sofosbuvir/ Velpatasvir/ Voxilaprevir	ATV (unboosted), ATV/c, ATV/r	When Given with ATV/r: • Voxilaprevir AUC ↑ 4.3-fold • Velpatasvir AUC ↑ 93% • Sofosbuvir AUC ↑ 40%	**Do not coadminister.**
	LPV/r	↑ voxilaprevir expected	**Do not coadminister.**
	DRV/r, DRV/c	When Given with DRV/r: • 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	**Do not coadminister.**
Herbal Products			
St. John's Wort	All PIs	↓ PI expected	**Contraindicated.**
Hormonal Therapies			
Hormonal Contraceptives Oral	ATV (unboosted)	Ethinyl estradiol AUC ↑ 48% Norethindrone AUC ↑ 110%	Prescribe oral contraceptive that contains no more than 30 mcg of ethinyl estradiol or recommend alternative contraceptive method. Oral contraceptives containing less than 25 mcg of ethinyl estradiol or progestins other than norethindrone or norgestimate have not been studied.[c]

Table 18a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 12 of 17)

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hormonal Therapies, continued			
Hormonal Contraceptives Oral	ATV/r	Ethinyl estradiol AUC ↓ 19% and C_{min} ↓ 37% Norgestimate ↑ 85% Norethindrone AUC ↑ 51% and C_{min} ↑ 67%	Oral contraceptive should contain at least 35 mcg of ethinyl estradiol.[b] Oral contraceptives containing progestins other than norethindrone or norgestimate have not been studied.
	ATV/c	Drospirenone AUC ↑ 2.3-fold Ethinyl estradiol AUC ↓ 22%	**Contraindicated with drosperinone-containing hormonal contraceptive. Do not coadminister due to potential for hyperkalemia.** 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% With TPV/r: norethindrone AUC ↔	Consider alternative or additional contraceptive method or alternative ARV drug.
Depot Medroxy-progesterone Acetate (MPA) Injectable	LPV/r	MPA AUC ↑ 46% C_{min}: no significant change	No dose adjustment necessary.
Etonogestrel-Releasing Subdermal Implant	LPV/r	Etonogestrel AUC ↑ 52% and C_{min} ↑ 34%	Use standard dose.
	All other PIs	No data	Consider alternative or additional contraceptive method or alternative ARV drug.
Transdermal Ethinyl Estradiol/ Norelgestromin	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.
Menopausal Hormone Replacement Therapy	All PIs	With estradiol or conjugated estrogen (equine and synthetic): ↓ estrogen possible	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.

Table 18a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 13 of 17)

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hormonal Therapies, continued			
Gender-Affirming Hormone Therapy	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.
HMG-CoA Reductase Inhibitors			
Atorvastatin	ATV, 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_{max} ↑ 18.9-fold	**Coadministration is not recommended.**
	DRV/r	DRV/r + 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_{max} ↑ 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_{max} ↑ 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_{max} ↑ 8.6-fold	**Do not coadminister.**
Lovastatin	All PIs	Significant ↑ lovastatin expected	**Contraindicated.**
Pitavastatin	All PIs	ATV ↑ pitavastatin AUC 31%, C_{max} ↑ 60% ↔ ATV DRV/r ↓ pitavastatin AUC 26% ↔ DRV/r LPV/r ↓ pitavastatin AUC 20% ↔ LPV	No dose adjustment necessary.
Pravastatin	ATV/c, ATV/r	No data	Titrate pravastatin dose carefully while monitoring for toxicities.
	DRV/c, DRV/r	With DRV/r, Pravastatin AUC: • ↑ 81% following single dose of pravastatin • ↑ 23% at steady state	Titrate pravastatin dose carefully while monitoring for toxicities.
	LPV/r	Pravastatin AUC ↑ 33%	No dose adjustment necessary.

Table 18a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 14 of 17)

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
HMG-CoA Reductase Inhibitors, continued			
Rosuvastatin	ATV/r	Rosuvastatin AUC ↑ 3-fold, C_{max} ↑ 7-fold	Titrate rosuvastatin dose carefully and use lowest dose necessary while monitoring for toxicities. Do not exceed 10 mg rosuvastatin daily.
	ATV/c	Rosuvastatin AUC ↑ 3.4-fold, C_{max} ↑ 10.6-fold	
	DRV/c	Rosuvastatin AUC ↑ 1.9-fold, C_{max} ↑ 3.8-fold	Titrate rosuvastatin dose carefully and use the lowest necessary dose while monitoring for toxicities. Do not exceed 20 mg rosuvastatin daily.
	DRV/r	Rosuvastatin AUC ↑ 48%, C_{max} ↑ 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_{max} ↑ 4.7-fold	Titrate rosuvastatin dose carefully and use the lowest necessary dose. Do not exceed 10 mg rosuvastatin daily.
	TPV/r	Rosuvastatin AUC ↑ 26%, C_{max} ↑ 2.2-fold	No dose adjustment necessary.
Simvastatin	All PIs	Significant ↑ simvastatin expected	**Contraindicated.**
Immunosuppressants			
Cyclosporine, Everolimus, Sirolimus, Tacrolimus	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.
Narcotics and Treatment for Opioid Dependence			
Buprenorphine Sublingual, buccal, or implant	ATV (unboosted)	Buprenorphine AUC ↑ 93% Norbuprenorphine[d] AUC ↑ 76% ↓ ATV possible	**Do not coadminister buprenorphine with unboosted ATV.**
	ATV/r	Buprenorphine AUC ↑ 66% Norbuprenorphine[d] 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.
	ATV/c, DRV/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.
	DRV/r	Buprenorphine: no significant effect Norbuprenorphine[d] AUC ↑ 46%, C_{min} ↑ 71%	No dose adjustment necessary. Clinical monitoring is recommended. When transferring buprenorphine from transmucosal to implantation, monitor to ensure buprenorphine effect is adequate and not excessive.
	LPV/r	No significant effect	
	TPV/r	Buprenorphine: no significant effect Norbuprenorphine[d] AUC, C_{max}, and C_{min} ↓ 80% TPV C_{min} ↓ 19%–40%	Consider monitoring TPV level. When transferring buprenorphine from transmucosal to implantation, monitor to ensure buprenorphine effect is adequate and not excessive.

Table 18a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 15 of 17)

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Narcotics and Treatment for Opioid Dependence, continued			
Fentanyl	All PIs	↑ fentanyl possible	Clinical monitoring is recommended, including for potentially fatal respiratory depression.
Methadone	ATV (unboosted)	No significant effect	No dose adjustment necessary.
	ATV/c, DRV/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[e] AUC 16%–18% LPV/r ↓ methadone AUC 26% to 53% TPV/r ↓ R-methadone[e] 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.
Oxycodone	All PIs	Oxycodone AUC ↑ 2.6-fold with LPV/r	Monitor for opioid-related adverse effects. Oxycodone dose reduction may be necessary.
Tramadol	ATV/c, DRV/c	↑ tramadol possible	Tramadol dose reduction may be necessary. Monitor for tramadol toxicities and clinical response.
Phosphodiesterase Type 5 (PDE5) Inhibitors			
Avanafil	All PIs except unboosted ATV	RTV (600 mg BID for 5 days) ↑ avanafil AUC 13-fold, C_{max} 2.4-fold	**Coadministration is not recommended.**
	ATV (unboosted)	No data	Avanafil dose should not exceed 50 mg once every 24 hours.
Sildenafil	All PIs	DRV/r + sildenafil 25 mg similar to sildenafil 100 mg alone RTV 500 mg BID ↑ sildenafil AUC 1000%	For Treatment of Erectile Dysfunction: • Start with sildenafil 25 mg every 48 hours and monitor for adverse effects of sildenafil. For Treatment of PAH: • **Contraindicated.**
Tadalafil	All PIs	RTV 200 mg BID ↑ tadalafil AUC 124% TPV/r (1st dose) ↑ tadalafil AUC 133% TPV/r steady state: no significant effect	For Treatment of Erectile Dysfunction: • Start with tadalafil 5-mg dose and do not exceed a single dose of 10 mg every 72 hours. Monitor for adverse effects of tadalafil. For Treatment of PAH: *In patients on a PI >7 days:* • Start with tadalafil 20 mg once daily and increase to 40 mg once daily based on tolerability. *In patients on tadalafil who require a PI:* • Stop tadalafil ≥24 hours before PI initiation. Seven days after PI initiation, restart tadalafil at 20 mg once daily and increase to 40 mg once daily based on tolerability. *In patients switching between COBI and RTV:* • Maintain tadalafil dose. For Treatment of Benign Prostatic Hyperplasia: • Maximum recommended daily dose is 2.5 mg per day.

Table 18a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 16 of 17)

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Phosphodiesterase Type 5 (PDE5) Inhibitors, continued			
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.
Sedative/Hypnotics			
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	**Do not coadminister oral midazolam and PIs.** Parenteral midazolam can be used with caution when given as a single dose in a monitored situation for procedural sedation.
Suvorexant	All PIs	↑ suvorexant expected	**Coadministration is not recommended.**
Triazolam	All PIs	↑ triazolam expected RTV (200 mg BID) ↑ triazolam half-life 1200% and AUC 2000%	**Contraindicated.**
Zolpidem	PI/r, ATV/c, DRV/c	↑ zolpidem possible	Initiate zolpidem at a low dose. Dose reduction may be necessary.
Miscellaneous Drugs			
Alfuzosin	All PIs	↑ alfuzosin expected	**Contraindicated.**
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	**Contraindicated.**
Colchicine	All PIs	RTV 100 mg BID ↑ colchicine AUC 296%, C_{max} 184% With all PIs with or without COBI or RTV: significant ↑ colchicine expected	For Treatment of Gout Flares: • Colchicine 0.6 mg x 1 dose, followed by 0.3 mg 1 hour later. Do not repeat dose for at least 3 days. For Prophylaxis of Gout Flares: • Colchicine 0.3 mg once daily or every other day. For Treatment of Familial Mediterranean Fever: • Do not exceed colchicine 0.6 mg once daily or 0.3 mg BID. **Do not coadminister in patients with hepatic or renal impairment.**
Dronabinol	All PIs	↑ dronabinol possible	Monitor for increased dronabinol-related adverse reactions.
Eluxadoline	All PIs	↑ eluxadoline expected	Administer eluxadoline at a dose of 75 mg twice daily and monitor for eluxadoline-related adverse effects.
Ergot Derivatives	All PIs	↑ dihydroergotamine, ergotamine, methylergonovine expected	**Contraindicated.**

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

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

[a] DHA is an active metabolite of artemether.

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

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

[d] Norbuprenorphine is an active metabolite of buprenorphine.

[e] 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_{max} = maximum plasma concentration; C_{min} = minimum plasma concentration; CNS = central nervous system; COBI, c = cobicistat; CrCl = creatinine clearance; CV = cardiovascular; CYP = cytochrome P; DHA = dihydroartemisinin; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; ECG = electrocardiogram; eGFR = estimated glomerular filtration rate; HCV = hepatitis C virus; HRT = hormone replacement therapy; INR = international normalized ratio; LPV = lopinavir; LPV/r = ritonavir-boosted lopinavir; MPA = medroxyprogesterone acetate; PAH = pulmonary arterial hypertension; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; PK = pharmacokinetic; PPI = proton pump inhibitor; PTH = parathyroid hormone; QTc = QT corrected for heart rate; RTV, r = ritonavir; TCA = tricyclic antidepressant; TDF = tenofovir disoproxil fumarate; TPV = tipranavir; TPV/r = tipranavir/ritonavir; VPA = valproic acid

Table 18b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 1 of 9)

This table provides information relating to PK interactions between NNRTIs and non-ARV drugs. For interactions between ARV agents and for dosing recommendations, refer to Tables 18c, 19a, and 19b. Recommendations for managing a particular drug interaction may differ depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or if a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly.

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

Concomitant Drug Class/ Name	NNRTI[a]	Effect on NNRTI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers			
Antacids	RPV	↓ RPV expected when given simultaneously	Give antacids at least 2 hours before or at least 4 hours after RPV.
H2 Receptor Antagonists	RPV	↓ RPV	Give H2 receptor antagonists at least 12 hours before or at least 4 hours after RPV.
PPIs	RPV	With Omeprazole 20 mg Daily: • RPV AUC ↓ 40%, C_{min} ↓ 33%	**Contraindicated. Do not coadminister.**
Anticoagulants/Antiplatelets			
Apixaban	EFV, ETR, NVP	↓ apixaban possible	Consider alternative therapy.
Betrixaban	EFV, NVP, RPV	↔ betrixaban expected	No dose adjustment necessary.
	ETR	↑ betrixaban possible	Consider alternative therapy. If coadministration is necessary, reduce betrixaban initial dose to 80 mg, followed by 40 mg daily. Monitor for betrixaban toxicity.
Clopidogrel	ETR	↓ activation of clopidogrel possible	ETR may prevent metabolism of clopidogrel (inactive) to its active metabolite. Avoid coadministration, if possible.
	NVP, RPV	↔ clopidogrel expected	No dose adjustment necessary.
Dabigatran	EFV, NVP, RPV	↔ dabigatran expected	No dose adjustment necessary.
	ETR	↑ dabigatran possible	Consider alternative therapy. If coadministration is necessary, monitor for dabigatran toxicity.
Edoxaban	EFV, NVP, RPV	↔ edoxaban expected	No dose adjustment necessary.
	ETR	↑ edoxaban possible	Consider alternative therapy. If coadministration is necessary, monitor for edoxaban toxicity.
Prasugrel	EFV, ETR, NVP, RPV	↔ prasugrel expected	No dose adjustment necessary.
Rivaroxaban	EFV, ETR, NVP	↓ rivaroxaban possible	Consider alternative therapy.
Ticagrelor	EFV, ETR, NVP	↓ ticagrelor expected	Consider alternative therapy.
Warfarin	EFV, ETR, NVP	↑ or ↓ warfarin possible	Monitor INR and adjust warfarin dose accordingly.

Table 18b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 2 of 9)

Concomitant Drug Class/ Name	NNRTI[a]	Effect on NNRTI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Anticonvulsants			
Carbamazepine, Phenobarbital, Phenytoin	EFV	Carbamazepine + EFV: • Carbamazepine AUC ↓ 27% • EFV AUC ↓ 36% Phenytoin + EFV: • ↓ EFV • ↓ phenytoin possible	Monitor anticonvulsant and EFV levels or, if possible, use alternative anticonvulsant to those listed.
	ETR	↓ anticonvulsant and ETR possible	**Do not coadminister.** Consider alternative anticonvulsant.
	NVP	↓ anticonvulsant and NVP possible	Monitor anticonvulsant and NVP levels and virologic responses or consider alternative anticonvulsant.
	RPV	↓ RPV possible	**Contraindicated. Do not coadminister.** Consider alternative anticonvulsant.
Eslicarbazepine	EFV, ETR, NVP, RPV	↓ NNRTI possible	Monitor virologic outcomes and consider monitoring plasma concentrations of ARVs, or consider alternative anticonvulsant or ARV drug.
Oxcarbazepine	RPV	↓ RPV possible	**Contraindicated. Do not coadminister.** 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.
Antidepressants			
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	EFV, ETR, NVP, RPV	↔ antidepressant expected	No dose adjustment necessary.
Paroxetine	EFV, ETR, NVP, RPV	↔ paroxetine observed with EFV or ETR ↔ expected with 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.
	RPV	↑ RPV possible	
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 18b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 3 of 9)

Concomitant Drug Class/ Name	NNRTI[a]	Effect on NNRTI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antifungals			
Fluconazole	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.
	RPV	↑ RPV possible	No dose adjustment necessary.
Isavuconazole	EFV, ETR, NVP	↓ isavuconazole possible	Dose adjustments for isavuconazole may be necessary. Consider monitoring isavuconazole level and antifungal response.
	RPV	↑ RPV possible	No dose adjustment necessary.
Itraconazole	EFV	Itraconazole and OH-itraconazole AUC, C_{max}, and C_{min} ↓ 35%–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.
	RPV	↑ RPV possible	No dose adjustment necessary.
Posaconazole	EFV	Posaconazole AUC ↓ 50% ↔ EFV	Avoid concomitant use unless the benefit outweighs the risk. If coadministered, monitor posaconazole concentration and adjust dose accordingly.
	ETR, NVP, RPV	↑ NNRTI possible	Monitor for NNRTI toxicities.
Voriconazole	EFV	Voriconazole AUC ↓ 77% EFV AUC ↑ 44%	**Contraindicated at standard doses.** Dose Adjustment: • Voriconazole 400 mg BID, EFV 300 mg daily
	ETR	Voriconazole AUC ↑ 14% ETR AUC ↑ 36%	No dose adjustment necessary; use with caution. Consider monitoring voriconazole level.
	NVP	↓ voriconazole possible ↑ NVP possible	Monitor for toxicity and antifungal response and/or voriconazole level.
	RPV	↑ RPV possible	No dose adjustment necessary.
Antihyperglycemics			
Canagliflozin, Dapagliflozin, Empagliflozin, Sitagliptin	EFV, ETR, NVP, RPV	↔ antihyperglycemic expected	No dose adjustment necessary.
Linagliptin, Saxagliptin	EFV, ETR, NVP	↓ antihyperglycemic possible	Monitor glycemic control.

Table 18b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 4 of 9)

Concomitant Drug Class/ Name	NNRTI[a]	Effect on NNRTI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antimalarials			
Artemether/ Lumefantrine	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 and malaria recurrence.
	ETR	Artemether AUC ↓ 38% DHA AUC ↓ 15% Lumefantrine AUC ↓ 13% ETR AUC ↑ 10%	Clinical significance of the reduced antimalarial drug concentrations unknown. If used in combination with ETR, monitor closely for antimalarial efficacy.
	NVP	Artemether AUC ↓ 67%–72% DHA: • Study results are conflicting. AUC ↓ 37% in one study, no difference in another. Lumefantrine: • Study results are conflicting. Lumefantrine AUC ↓ 25%– 58% in 2 studies but ↑ 56% in another.	Clinical significance unknown. If used, monitor closely for antimalarial efficacy and lumefantrine toxicity.
Atovaquone/ Proguanil	EFV	Atovaquone AUC ↓ 75% Proguanil AUC ↓ 43%	No dose recommendation. Consider alternative drug for malaria prophylaxis, if possible.
Antimycobacterials			
Bedaquiline	EFV, ETR	↓ bedaquiline possible	**Do not coadminister.**
	NVP	↔ bedaquiline AUC	No dose adjustment necessary.
Clarithromycin	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.
Rifabutin	EFV	Rifabutin ↓ 38%	Dose: • 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 ↓ 17% ETR AUC ↓ 37%	**If ETR is used with an RTV-boosted PI, rifabutin should not be coadministered.** Dose: • Rifabutin 300 mg once daily if ETR is not coadministered with a PI/r.

Table 18b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 5 of 9)

Concomitant Drug Class/ Name	NNRTI[a]	Effect on NNRTI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antimycobacterials			
Rifabutin, continued	NVP	Rifabutin AUC ↑ 17% and metabolite AUC ↑ 24% NVP C_{min} ↓ 16%	No dose adjustment necessary. Use with caution.
	RPV	Rifabutin + RPV 50 mg once daily compared to RPV 25 mg once daily alone: ↔ RPV AUC, C_{min}	Increase RPV dose to 50 mg once daily.
Rifampin	EFV	EFV AUC ↓ 26%	Maintain EFV dose at 600 mg once daily and monitor for virologic response. Consider therapeutic drug monitoring.
	ETR	Significant ↓ ETR possible	**Do not coadminister.**
	NVP	NVP ↓ 20%–58%	**Do not coadminister.**
	RPV	RPV AUC ↓ 80%	**Contraindicated. Do not coadminister.**
Rifapentine	EFV	↔ EFV concentrations	No dose adjustment necessary.
	ETR, NVP	↓ NNRTI possible	**Do not coadminister.**
	RPV	↓ RPV expected	**Contradindicated.**
Antipneumocystis and Antitoxoplasmosis Drugs			
Atovaquone	EFV	Atovaquone AUC ↓ 44%–47%	Consider alternative agent for PCP or toxoplasmosis treatment or use alternative ARV drug. If used in combination, monitor therapeutic efficacy of atovaquone.
Antipsychotics			
Olanzapine	EFV	↓ olanzapine possible	Monitor effect of olanzapine.
	ETR, NVP, RPV	↔ olanzapine expected	No dose adjustment necessary.
Pimozide	EFV	↑ pimozide possible	**Coadministration is not recommended.** Consider alternative antipsychotic.
	ETR, NVP	↓ pimozide possible	Monitor effect of pimozide.
Lurasidone, Quetiapine, Thioridazine	EFV, ETR, NVP	↓ antipsychotic possible	Monitor effect of antipsychotic.
Benzodiazepines			
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 C_{max} ↑ 16%, AUC ↔	No dose adjustment necessary.
Midazolam	EFV	Significant ↑ midazolam expected	**Do not coadminister with oral midazolam.** Parenteral midazolam can be used with caution as a single dose and can be given in a monitored situation for procedural sedation.
Triazolam	EFV	Significant ↑ triazolam expected	**Do not coadminister.**

Table 18b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 6 of 9)

Concomitant Drug Class/ Name	NNRTI[a]	Effect on NNRTI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Cardiac Medications			
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.
	NVP	↓ diltiazem or verapamil possible	
Corticosteroids			
Dexamethasone	EFV, ETR, NVP	↓ EFV, ETR, and NVP possible	Consider alternative corticosteroid for long-term use. If dexamethasone is used with NNRTI, monitor virologic response.
	RPV	Significant ↓ RPV possible	**Contraindicated with more than a single dose of dexamethasone.**
Hepatitis C Direct-Acting Antiviral Agents			
Daclatasvir	EFV, ETR, NVP	Daclatasvir 120 mg once daily + EFV 600 mg daily compared to daclatasvir 60 mg alone: daclatasvir C_{min} ↓ 17%, AUC ↑ 37%	The recommended dose is daclatasvir 90 mg once daily.
	RPV	No data	No dose adjustment necessary.
Dasabuvir + Paritaprevir/ Ombitasivir/RTV	EFV	No data	**Contraindicated.**
	ETR, NVP	↓ DAAs possible	**Do not coadminister.**
	RPV	RPV AUC ↑ 150%–225%	**Do not coadminister, due to potential for QT interval prolongation with higher concentrations of RPV.**
Elbasvir/ Grazoprevir	EFV	Elbasvir AUC ↓ 54% Grazoprevir AUC ↓ 83% EFV ↔ by grazoprevir EFV ↔ AUC by elbasvir	**Contraindicated.**
	ETR, NVP	↓ elbasvir, grazoprevir expected	**Do not coadminister.**
	RPV	Elbasvir, grazoprevir, and RPV ↔	No dose adjustment necessary.
Glecaprevir/ Pibrentasvir	EFV	↓ glecaprevir and pibrentasvir expected	**Do not coadminister.**
	NVP, ETR	↓ glecaprevir and pibrentasvir possible	
	RPV	↔ glecaprevir, pibrentasvir, and RPV AUC ↑ 84%	No dose adjustment necessary.
Ledipasvir/ Sofosbuvir	EFV	Ledipasvir AUC, C_{min}, and $C_{max:}$ all ↓ 34% Sofosbuvir: no significant effect	No dose adjustment necessary.
	ETR, NVP	No significant effect expected	
	RPV	Ledipasvir, sofosbuvir, and RPV ↔	

Table 18b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 7 of 9)

Concomitant Drug Class/ Name	NNRTI[a]	Effect on NNRTI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hepatitis C Direct-Acting Antiviral Agents, continued			
Simeprevir	EFV	Simeprevir AUC ↓ 71%, C_{min} ↓ 91% ↔ EFV	**Do not coadminister.**
	ETR, NVP	↓ simeprevir expected	**Do not coadminister.**
	RPV	↔ simeprevir and RPV	No dose adjustment necessary.
Sofosbuvir/ Velpatasvir	EFV	Velpatasvir AUC ↓ 43% , C_{max} ↓ 37% and C_{min} ↓ 47%	**Do not coadminister.**
	ETR, NVP	↓ velpatasvir expected	**Do not coadminister.**
	RPV	No significant effect expected	No dose adjustment necessary.
Sofosbuvir/ Velpatasvir/ Voxilaprevir	EFV	Velpatasvir AUC ↓ 43% , C_{max} ↓37% and C_{min} ↓47 ↓ voxilaprevir expected	**Do not coadminister.**
	ETR, NVP,	↓ voxilaprevir expected ↓ velpatasvir expected	**Do not coadminister.**
	RPV	No signficant effect expected	No dose adjustment necessary.
Herbal Products			
St. John's Wort	EFV, ETR, NVP, RPV	↓ NNRTI	**Contraindicated.**
Hormonal Therapies			
Hormonal Contraceptives	EFV	Ethinyl estradiol ↔ Levonorgestrel (metabolite of oral norgestimate) AUC ↓ 83% Norelgestromin (metabolite of oral norgestimate) AUC ↓ 64% Etonogestrel (metabolite of oral desogestrel) C_{min} ↓ 61% Etonogestrel (implant) AUC ↓ 63%–82% Levonorgestrel (implant) AUC ↓ 47%	Use alternative or additional contraceptive methods. Unintended pregnancies were observed in women who used EFV and levonorgestrel implant concomitantly.
		DMPA: no significant change	No dose adjustment necessary.
	ETR	Ethinyl estradiol AUC ↑ 22% Norethindrone: no significant effect	No dose adjustment necessary.
	NVP	Ethinyl estradiol AUC ↓ 29%, C_{min} ↓ 58% Norethindrone AUC ↓ 18% Etonogestrel (metabolite of oral desogestrel) C_{min} ↓ 22%	Based on clinical data demonstrating no change in effectiveness, no dose adjustment necessary.
		Etonogestrel (implant): no significant change	No dose adjustment necessary.
		DMPA: no significant change	No dose adjustment necessary.

Table 18b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 8 of 9)

Concomitant Drug Class/ Name	NNRTI[a]	Effect on NNRTI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hormonal Therapies, continued			
Hormonal Contraceptives, continued	NVP, continued	Levonorgestrel (implant) AUC ↑ 35%	No dose adjustment necessary.
	RPV	Ethinyl estradiol: no significant change Norethindrone: no significant change	No dose adjustment necessary.
Levonorgestrel For emergency contraception	EFV	Levonorgestrel AUC ↓ 58%	Effectiveness of emergency postcoital contraception may be diminished.
Menopausal Hormone Replacement Therapy	EFV, ETR, NVP	With estradiol or conjugated estrogen (equine and synthetic): ↓ estrogen possible ↓ medroxyprogesterone possible ↓ micronized progesterone possible ↓ drospirenone possible See Hormonal Contraceptives for other progestin-NNRTI interactions	Monitor menopausal symptoms. The lowest dose of hormonal therapy should be used to achieve menopausal symptom relief.
Gender-Affirming Hormone Therapy	EFV, ETR, NVP	↓ estradiol possible ↔ goserelin, leuprolide acetate, and spironolactone expected ↓ dutasteride and finasteride possible	Monitor feminizing effects of estrogen and antiandrogen therapy and adjust dosing as necessary.
	EFV, ETR, NVP	↓ testosterone possible	Monitor masculinizing effects of testosterone and adjust testosterone dose as necessary.
HMG-CoA Reductase Inhibitors			
Atorvastatin	EFV, ETR	Atorvastatin AUC ↓ 32%–43%	Adjust atorvastatin according to lipid responses, but do not exceed the maximum recommended dose.
	NVP	↓ atorvastatin possible	Adjust atorvastatin according to lipid responses, not to exceed the maximum recommended dose.
	RPV	Atorvastatin AUC ↔ Atorvastatin metabolites ↑ 23%–39%	No dose adjustment necessary.
Fluvastatin	EFV, ETR	↑ fluvastatin possible	Dose adjustments for fluvastatin may be necessary. Monitor for fluvastatin toxicity.
Lovastatin, Simvastatin	EFV	Simvastatin AUC ↓ 68% Simvastatin active metabolite AUC ↓ 60%	Adjust simvastatin dose according to lipid responses, but do not exceed the maximum recommended dose. If EFV is used with a PI/r, simvastatin and lovastatin should be avoided.
	ETR, NVP	↓ lovastatin possible ↓ simvastatin possible	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.

Table 18b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 9 of 9)

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

[a] Approved dose for RPV is 25 mg once daily. Most PK interaction studies were performed using 75 to 150 mg per dose.
[b] Norbuprenorphine is an active metabolite of buprenorphine.
[c] R-methadone is the active form of methadone.

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

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

Table 18c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents) (Last updated October 17, 2017; last reviewed October 17, 2017)
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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 if a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly.

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

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

Table 18c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents) (Last updated October 17, 2017; last reviewed October 17, 2017)
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Concomitant Drug Class/ Name	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosage Recommendations and Clinical Comments
Narcotics/Treatment for Opioid Dependence, continued			
Methadone	ABC	Methadone clearance ↑ 22%	No dose adjustment.
	ZDV	ZDV AUC ↑ 29%–43%	Monitor for ZDV-related adverse effects.
Other			
Atovaquone	ZDV	ZDV AUC ↑ 31%	Monitor for ZDV-related adverse effects.
Anticonvulsants Carbamazepine, oxcarbazepine, phenobarbital, phenytoin	TAF	With carbamazepine: • TAF AUC ↓ 55% ↓ TAF possible with other anticonvulsants	Consider alternative anticonvulsant.
Antimycobacterial Rifabutin, rifampin, rifapentine	TAF	↓ TAF possible	**Coadministration is not recommended.**
Herbal Products St. John's wort	TAF	↓ TAF possible	**Coadministration is not recommended.**
PIs (HIV)			
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_{min} ↓ 23% to 40% (higher C_{min} with RTV than without RTV) TDF AUC ↑ 24%–37%	**Avoid concomitant use without RTV or COBI.** Dose: • ATV 300 mg daily + (RTV 100 mg or COBI 150 mg) daily when coadministered with TDF 300 mg daily. • If using TDF and H2 receptor antagonist in ART-experienced patients, use ATV 400 mg daily + (RTV 100 mg or COBI 150 mg) daily. Monitor for TDF-associated toxicity.
	ZDV	With ATV (Unboosted): • ZDV C_{min} ↓ 30% and AUC ↔	Clinical significance unknown.
DRV/c	TAF	TAF 25 mg with DRV/c: • TAF ↔	No dose adjustment.
	TDF	↑ TDF possible	Monitor for TDF-associated toxicity.
DRV/r	TAF	TAF 10 mg with DRV/r: • TAF ↔	No dose adjustment.
	TDF	TDF AUC ↑ 22% and C_{min} ↑ 37%	Clinical significance unknown. Monitor for TDF toxicity.

Table 18c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents) (Last updated October 17, 2017; last reviewed October 17, 2017)
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Concomitant Drug Class/ Name	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosage Recommendations and Clinical Comments
PIs (HIV), continued			
LPV/r	TAF	TAF 10 mg with DRV/r: • TAF AUC ↑ 47%	No dose adjustment.
	TDF	LPV/r AUC ↓ 15% TDF AUC ↑ 34%	Clinical significance unknown. Monitor for TDF toxicity.
TPV/r	ABC	ABC AUC ↓ 35%–44%	Appropriate doses for this combination have not been established.
	TAF	↓ TAF expected	**Coadministration is not recommended.**
	TDF	TDF AUC ↔ TPV/r AUC ↓ 9%–18% and C_{min} ↓ 12%–21%	No dose adjustment.
	ZDV	ZDV AUC ↓ 35% TPV/r AUC ↓ 31%–43%	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; ATC/c = atazanavir/cobicistat; AUC = area under the curve; C_{min} = minimum plasma concentration; COBI, c = cobicistat; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; FTC = emtricitabine; HCV = hepatitis C virus; INSTI = integrase strand transfer inhibitors; LPV/r = lopinavir/ritonavir; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PI/r = ritonavir-boosted protease inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV, r = ritonavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV/r = tipranavir/ritonavir; ZDV = zidovudine

Table 18d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 1 of 11)

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

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers			
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).	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%–50% if given simultaneously with antacid EVG AUC ↓ 15%–20% if given 2 hours before or after antacid; ↔ with 4-hour interval	Separate EVG/c/TDF/FTC and antacid administration by more than 2 hours.
	RAL	Al-Mg Hydroxide Antacid: • RAL C_{min} ↓ 49% to 63% $CaCO_3$ Antacid: • RAL (400 mg BID) C_{min} ↓ 32% • RAL (1200 mg once daily) C_{min} ↓ 48% to 57%	**Do not coadminister RAL and Al-Mg hydroxide antacids.** Use alternative acid reducing agent. With $CaCO_3$ Antacids: • **RAL 1200 mg once daily: Do not coadminister** • RAL 400 mg BID: No dose adjustment or separation necessary
H2-Receptor Antagonists	EVG/c	No significant effect	No dose adjustment.
Proton Pump Inhibitors (PPIs)	DTG	No significant effect	No dose adjustment.
	EVG/c	No significant effect	No dose adjustment.
	RAL	RAL AUC ↑ 37% and C_{min} ↑ 24%	No dose adjustment.
Anticoagulants and Antiplatelets			
Apixaban	EVG/c	↑ apixaban expected	**Coadministration is not recommended.** Consider alternative antiretroviral (e.g., an unboosted INSTI) or warfarin. If coadministration is necessary, reduce apixaban dose by 50% and monitor for apixaban toxicity.
Betrixaban	EVG/c	↑ betrixaban expected	**Coadministration is not recommended.** Consider alternative antiretroviral (e.g., an unboosted INSTI) or warfarin.
Dabigatran	EVG/c	↑ dabigatran expected Dabigatran AUC ↑ 110%–127% with COBI 150 mg alone	**Coadministration is not recommended.** Consider alternative antiretroviral (e.g., another INSTI) or warfarin.
Edoxaban	EVG/c	↑ edoxaban expected	**Coadministration is not recommended.** Consider alternative antiretroviral (e.g., an unboosted INSTI) or warfarin.

Table 18d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 2 of 11)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Anticoagulants and Antiplatelets, continued			
Rivaroxaban	EVG/c	↑ rivaroxaban expected	**Coadministration is not recommended.** Consider alternative antiretroviral (e.g., an unboosted INSTI) or warfarin.
Ticagrelor	EVG/c	↑ ticagrelor expected	**Avoid concomitant use.**
Vorapaxar	EVG/c	↑ vorapaxar expected	**Avoid concomitant use.**
Warfarin	EVG/c	↑ or ↓ warfarin possible	Monitor INR and adjust warfarin dose accordingly.
Anticonvulsants			
Carbamazepine	DTG	DTG AUC ↓ 49%	Increase DTG dose to 50 mg BID in treatment-naive or treatment-experienced, INSTI-naive patients. Use alternative anticonvulsant for INSTI-experienced patients with known or suspected INSTI resistance.
	EVG/c	Carbamazepine AUC ↑ 43% EVG AUC ↓ 69% and C_{min} ↓ >99% ↓ COBI expected	**Contraindicated.**
	RAL	↓ or ↔ RAL possible	**Coadministration is not recommended.**
Phenobarbital **Phenytoin**	DTG	↓ DTG possible	**Coadministration is not recommended.**
	EVG/c	↓ EVG/c expected	**Contraindicated.**
	RAL	↓ or ↔ RAL possible	**Coadministration is not recommended.**
Ethosuximide	EVG/c	↑ ethosuximide possible	Clinically monitor for ethosuxamide toxicities.
Oxcarbazepine	DTG, EVG/c	↓ INSTI possible ↓ cobicistat possible	Consider alternative anticonvulsant.
Antidepressants/Anxiolytics/Antipsychotics Also see Sedative/Hypnotics section below.			
Bupropion	EVG/c	↑ or ↓ bupropion possible	Titrate bupropion dose based on clinical response.
Buspirone	EVG/c	↑ buspirone possible	Initiate buspirone at a low dose. Dose reduction may be necessary.
Fluvoxamine	EVG/c	↑ or ↓ EVG possible	Consider alternative antidepressant or ARV.
Lurasidone	EVG/c	↑ lurasidone expected	**Contraindicated.**
Pimozide	EVG/c	↑ pimozide expected	**Contraindicated.**
Quetiapine	EVG/c	↑ quetiapine AUC expected	Initiation of Quetiapine in a Patient Receiving EVG/c: • Start quetiapine at the lowest dose and titrate up as needed. Monitor for quetiapine efficacy and adverse effects. Initiation of EVG/c in a Patient Receiving a Stable Dose of Quetiapine: • Reduce quetiapine dose to 1/6 of the original dose, and closely monitor for quetiapine efficacy and adverse effects.

Table 18d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 3 of 11)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antidepressants/Anxiolytics/Antipsychotics Also see Sedative/Hypnotics section below.			
Selective Serotonin Reuptake Inhibitors (SSRIs) Citalopram, escitalopram, fluoxetine, paroxetine, sertraline	EVG/c	↔ EVG ↔ sertraline	No dose adjustment necessary.
		↑ other SSRI possible	Initiate with lowest dose of SSRI and titrate dose carefully based on antidepressant response.
	RAL	↔ RAL ↔ citalopram ↔ SSRI expected	No dose adjustment necessary.
	DTG	↔ DTG ↔ citalopram ↔ SSRI expected	No dose adjustment necessary.
Tricyclic Antidepressants (TCAs) Amitriptyline, desipramine, doxepin, imipramine, nortriptyline	EVG/c	Desipramine AUC ↑ 65%	Initiate with lowest dose of TCA and titrate dose carefully.
		↑ TCA expected	Initiate with lowest dose of TCA and titrate dose carefully based on antidepressant response and/or drug levels.
Trazodone	EVG/c	↑ trazodone possible	Initiate with lowest dose of trazodone and titrate dose carefully.
Antifungals			
Isavuconazole	EVG/c	↑ isavuconazole expected ↑ EVG and COBI possible	If coadministered, consider monitoring isavuconazole concentrations and assess virologic response.
Itraconazole	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	EVG/c	↑ EVG and COBI possible ↑ posaconazole possible	If coadministered, monitor posaconazole concentrations.
Voriconazole	EVG/c	↑ voriconazole expected ↑ EVG and COBI possible	Risk/benefit ratio should be assessed to justify use of voriconazole. If administered, consider monitoring voriconazole level. Adjust dose accordingly.
Antihyperglycemics			
Saxagliptin	EVG/c	↑ saxagliptin expected	Limit saxagliptin dose to 2.5 mg once daily.
Dapagliflozin/ Saxagliptin	EVG/c	↑ saxagliptin expected	Do not coadminister, as this coformulated drug contains 5 mg of saxagliptin.
Antimycobacterials			
Clarithromycin	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 18d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 4 of 11)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antimycobacterials, continued			
Rifabutin	DTG	Rifabutin (300 mg Once Daily): • DTG AUC ↔ and C_{min} ↓ 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%, C_{min} ↓ 67%	**Do not coadminister.**
	RAL	RAL AUC ↑ 19%, C_{min} ↓ 20%	No dose adjustment necessary.
Rifampin	DTG	Rifampin with DTG 50 mg BID Compared to DTG 50 mg BID Alone: • DTG AUC ↓ 54%, C_{min} ↓ 72% Rifampin with DTG 50 mg BID Compared to DTG 50 mg Once Daily Alone: • DTG AUC ↑ 33%, C_{min} ↑ 22%	Dose: • 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	Contraindicated.
	RAL	RAL 400 mg: • RAL AUC ↓ 40%, C_{min} ↓ 61% Rifampin with RAL 800 mg BID Compared to RAL 400 mg BID Alone: • RAL AUC ↑ 27%, C_{min} ↓ 53%	Dose: • RAL 800 mg BID, instead of 400 mg BID **Do not coadminister RAL 1200 mg once daily with rifampin.** Monitor closely for virologic response or consider using rifabutin as an alternative rifamycin.
Rifapentine	DTG	Significant ↓ DTG expected	**Do not coadminister.**
	EVG/c	Significant ↓ EVG and COBI expected	**Do not coadminister.**
	RAL	Rifapentine 900 mg Once Weekly: • RAL AUC ↑ 71%, C_{min} ↓ 12% Rifapentine 600 mg Once Daily: • RAL C_{min} ↓ 41%	For once-weekly rifapentine, use standard RAL 400 mg BID doses. **Do not coadminister with once-daily rifapentine.**
Cardiac Medications			
Antiarrhythmics Amiodarone, bepridil, digoxin, disopyramide, dronedarone, flecainide, systemic lidocaine, mexilitine, propafenone, quinidine	EVG/c	↑ antiarrhythmics possible Digoxin C_{max} ↑ 41% and no significant change in AUC	Use antiarrhythmics with caution. Therapeutic drug monitoring, if available, is recommended for antiarrhythmics.

Table 18d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 5 of 11)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Cardiac Medications			
Bosentan	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.
Beta-blockers (e.g., metoprolol, timolol)	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).
Calcium Channel Blockers (CCBs)	EVG/c	↑ CCBs possible	Coadminister with caution. Titrate CCB dose and monitor for CCB efficacy and toxicities. Refer to Table 18a for diltiazem + ATV/r recommendations.
Dofetilide	DTG	↑ dofetilide expected	**Contraindicated.**
Eplerenone	EVG/c	↑ eplerenone expected	**Contraindicated.**
Ranolazine	EVG/c	↑ ranolazine expected	**Contraindicated.**
Ivabradine	EVG/c	↑ ivabradine expected	**Contraindicated.**
Corticosteroids			
Beclomethasone Inhaled or intranasal	EVG/c	↔ expected	No dose adjustment necessary.
Budesonide, Ciclesonide, Fluticasone, Mometasone Inhaled or intranasal	EVG/c	↑ glucocorticoid possible	Coadministration can result in adrenal insufficiency and Cushing's syndrome. **Do not coadminister unless potential benefits of inhaled or intranasal corticosteroid outweigh the risks of systemic corticosteroid adverse effects.** Consider an alternative corticosteroid (e.g., beclomethasone).
Betamethasone, Budesonide Systemic	EVG/c	↑ glucocorticoids possible ↓ PI possible	Coadministration can result in adrenal insufficiency and Cushing's syndrome. **Do not coadminister unless potential benefits of systemic budesonide outweigh the risks of systemic corticosteroid adverse effects.**
Dexamethasone Systemic	EVG/c	↓ EVG and COBI possible	Consider an alternative corticosteroid for long-term use or alternative ART. If coadministration is necessary, monitor virologic response to ART.
Prednisone, Prednisolone Systemic	EVG/c	↑ prednisolone possible	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.

Table 18d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 6 of 11)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Corticosteroids, continued			
Betamethasone, Methylprednisolone, Prednisolone, Triamcinolone Local injections, including intra-articular, epidural, or intra-orbital	EVG/c	↑ glucocorticoids expected	**Do not coadminister.** Coadministration may result in adrenal insufficiency and Cushing's syndrome.
Hepatitis C Direct Acting Antivirals			
Daclatasvir	DTG	↔ daclatasvir	No dose adjustment necessary.
	EVG/c	↑ daclatasvir	Decrease daclastavir dose to 30 mg once daily.
	RAL	No data	No dose adjustment necessary.
Dasabuvir + Ombitasvir/ Paritaprevir/r	DTG	No data	No dosing recommendations at this time.
	EVG/c	No data	**Do not coadminister.**
	RAL	RAL AUC ↑ 134%	No dose adjustment necessary.
Elbasvir/Grazoprevir	DTG	↔ elbasvir ↔ grazoprevir ↔ DTG	No dose adjustment necessary.
	EVG/c	↑ elbasvir, grazoprevir expected	**Coadministration is not recommended.**
	RAL	↔ elbasvir ↔ grazoprevir RAL ↔ with elbasvir RAL AUC ↑ 43% with grazoprevir	No dose adjustment necessary.
Glecaprevir/ Pibrentasvir	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	**Do not coadminister.**
	EVG/c/ TAF/ FTC	↔ EVG/c/TAF/FTC expected	No dose adjustment necessary.
	DTG, RAL	↔ DTG or RAL	No dose adjustment necessary.
Simeprevir	DTG	↔ expected	No dose adjustment necessary.
	EVG/c	↑ simeprevir expected	**Coadministration is not recommended.**
	RAL	↔ expected	No dose adjustment necessary.
Sofosbuvir	All INSTIs	↔ expected	No dose adjustment necessary.
Sofosbuvir/Velpatasvir	All INSTIs	↔ expected	No dose adjustment necessary.

Table 18d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 7 of 11)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hepatitis C Direct Acting Antivirals, continued			
Sofosbuvir/ Velpatasvir/ Voxilaprevir	EVG/c	When Given with Sofosbuvir/Velpatasvir/ Voxilaprevir (400/100/100 mg) + Voxilaprevir 100 mg: • Sofosbuvir AUC ↑ 22% • ↔ velpatasvir • Voxilaprevir AUC ↑ 2-fold	No dose adjustment necessary.
	DTG, RAL	↔ expected	No dose adjustment necessary.
Herbal Products			
St. John's Wort	DTG	↓ DTG possible	**Do not coadminister.**
	EVG/c	↓ EVG and COBI possible	**Contraindicated.**
Hormonal Therapies			
Hormonal Contraceptives	DTG, RAL	↔ ethinyl estradiol, norgestimate, and DTG or RAL	No dose adjustment necessary.
	EVG/c	Norgestimate AUC, C_{max}, and C_{min} ↑ >2-fold Ethinyl estradiol AUC ↓ 25% and C_{min} ↓ 44%	The effects of increases in progestin (norgestimate) are not fully known and can include insulin resistance, dyslipidemia, acne, and venous thrombosis. Weigh the risks and benefits of the drug, and consider alternative contraceptive method.
		↑ drospirenone possible	Clinical monitoring is recommended, due to the potential for hyperkalemia.
Menopausal Hormone Replacement Therapy	DTG, RAL	With estradiol or conjugated estrogen (equine and synthetic): ↓ estrogen possible ↔ drospirenone, medroxyprogesterone, or micronized progesterone expected	No dose adjustment necessary.
	EVG/c	↓ estrogen possible ↑ drospirenone possible ↑ oral medroxyprogesterone possible ↑ oral micronized progesterone possible	Adjust estrogen and progestin dose as needed based on clinical effects.
Gender-Affirming Hormone Therapy	DTG, RAL	↔ estrogen expected	No dose adjustment necessary.
	DTG, EVG/c, RAL	↔ finasteride, goserelin, leuprolide acetate, spironolactone expected	
	EVG/c	↓ estradiol possible ↑ dutasteride possible	Adjust dutasteride dosage as needed based on clinical effects and endogenous hormone concentrations.
	EVG/c	↑ testosterone possible	Monitor masculinizing effects of testosterone and for adverse effects and adjust testosterone dose as necessary.
	DTG, RAL	↔ testosterone expected	No dose adjustment necessary.

Table 18d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 8 of 11)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
HMG-CoA Reductase Inhibitors			
Atorvastatin	EVG/c	↑ atorvastatin AUC 2.6-fold and C_{max} 2.3-fold	Titrate statin dose carefully and use the lowest dose necessary while monitoring for toxicities. Do not exceed 20 mg atorvastatin daily.
Lovastatin	EVG/c	Significant ↑ lovastatin expected	**Contraindicated**.
Pitavastatin, Pravastatin	EVG/c	No data	No dosage recommendation
Rosuvastatin	EVG/c	Rosuvastatin AUC ↑ 38% and C_{max} ↑ 89%	Titrate statin dose carefully and use the lowest dose necessary while monitoring for toxicities.
Simvastatin	EVG/c	Significant ↑ simvastatin expected	**Contraindicated**.
Immunosuppressants			
Cyclosporine, Everolimus, Sirolimus, Tacrolimus	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 specialist as necessary.
Narcotics/Treatment for Opioid Dependence			
Buprenorphine Sublingual, buccal, or implant	EVG/c	Buprenorphine AUC ↑ 35%, C_{max} ↑ 12%, and C_{min} ↑ 66% Norbuprenorphine AUC ↑ 42%, C_{max} ↑ 24%, and C_{min} ↑ 57%	No dose adjustment necessary. Clinical monitoring is recommended. When transferring buprenorphine from transmucosal to implantation, monitor to ensure buprenorphine effect is adequate and not excessive.
	RAL	↔ observed (sublingual) ↔ expected (implant)	No dose adjustment necessary.
Methadone	DTG	No significant effect	No dose adjustment necessary.
	EVG/c	No significant effect	No dose adjustment necessary.
	RAL	No significant effect	No dose adjustment necessary.
Neuroleptics			
Perphenazine, Risperidone, Thioridazine	EVG/c	↑ neuroleptic possible	Initiate neuroleptic at a low dose. Decrease in neuroleptic dose may be necessary.
PDE5 Inhibitors			
Avanafil	EVG/c	No data	Coadministration is not recommended.
Sildenafil	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: • **Contraindicated.**

Table 18d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 9 of 11)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
PDE5 Inhibitors, continued			
Tadalafil	EVG/c	↑ tadalafil expected	For Treatment of Erectile Dysfunction: • Start with tadalafil 5-mg dose and do not exceed a single dose of 10 mg every 72 hours. Monitor for adverse effects of tadalafil. For Treatment of PAH: *In patients on EVG/c >7 days:* • Start with tadalafil 20 mg once daily and increase to 40 mg once daily based on tolerability. *In patients on tadalafil who require EVG/c:* • Stop tadalafil ≥24 hours before EVG/c initiation. Seven days after EVG/c initiation, restart tadalafil at 20 mg once daily, and increase to 40 mg once daily based on tolerability.
Vardenafil	EVG/c	↑ vardenafil expected	Start with vardenafil 2.5 mg every 72 hours and monitor for adverse effects of vardenafil.
Sedative/Hypnotics			
Clonazepam, Clorazepate, Diazepam, Estazolam, Flurazepam	EVG/c	↑ benzodiazepines possible	Dose reduction of benzodiazepine may be necessary. Initiate with low dose and clinically monitor. Consider alternative benzodiazepines to diazepam, such as lorazepam, oxazepam, or temazepam.
Midazolam, Triazolam	DTG	With DTG 25 mg: • midazolam AUC ↔	No dose adjustment necessary.
	EVG/c	↑ midazolam expected ↑ triazolam expected	**Contraindicated. Do not coadminister triazolam or oral midazolam and EVG/c.** Parenteral midazolam can be used with caution in a closely monitored setting. Consider dose reduction, especially if more than one dose is administered.
Suvorexant	EVG/c	↑ suvorexant expected	**Coadministration is not recommended.**
Zolpidem	EVG/c	↑ zolpidem expected	Initiate zolpidem at a low dose. Dose reduction may be necessary.
Miscellaneous Drugs			
Alfuzosin	EVG/c	↑ alfuzosin expected	**Contraindicated.**
Calcifediol	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	EVG/c	↑ cisapride expected	**Contraindicated.**

Table 18d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 10 of 11)

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

Table 18d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 17, 2017; last reviewed October 17, 2017) (page 11 of 11)

Key to Acronyms: Al = aluminum; ART = antiretroviral therapy; ARV = antiretroviral; AUC = area under the curve; BID = twice daily; Ca = calcium; $CaCO_3$ = calcium carbonate; CCB = calcium channel blocker; C_{max} = maximum plasma concentration; C_{min} = minimum plasma concentration; COBI, c = cobicistat; CrCl = creatinine clearance; CYP = cytochrome P; DTG = dolutegravir; EVG = elvitegravir; Fe = iron; FTC = emtricitabine; GI = gastrointestinal; INR= international normalized ratio; INSTI = integrase strand transfer inhibitor; Mg = magnesium; PAH = pulmonary arterial hypertension; PI = protease inhibitor; PI/r = ritonavir-boosted protease inhibitor; PPI = proton pump inhibitor; PTH = parathyroid hormone; r = ritonavir; RAL = raltegravir; TDF = tenofovir disoproxil fumarate; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant; Zn = zinc

Table 18e. Drug Interactions between CCR5 Antagonist (Maraviroc) and Other Drugs (Including Antiretroviral Agents) (Last updated October 17, 2017; last reviewed October 17, 2017) (page 1 of 3)

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

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

Table 18e. Drug Interactions between CCR5 Antagonist (Maraviroc) and Other Drugs (Including Antiretroviral Agents) (Last updated October 17, 2017; last reviewed October 17, 2017) (page 2 of 3)

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

Table 18e. Drug Interactions between CCR5 Antagonist (Maraviroc) and Other Drugs (Including Antiretroviral Agents) (Last updated October 17, 2017; last reviewed October 17, 2017) (page 3 of 3)

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

Key to Symbols:

↑ = increase

↓ = decrease

↔ = no change

Key to Acronyms: ARV = antiretroviral; ATV = atazanavir; AUC = area under the curve; BID = twice daily; COBI = cobicistat; CYP = cytochrome P; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; INSTI = integrase strand transfer inhibitor; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; RAL = raltegravir; RTV = ritonavir; TPV = tipranavir; TPV/r = tipranavir/ritonavir

Table 19a. Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors[a] (Last updated October 17, 2017; last reviewed October 17, 2017) (Page 1 of 2)

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

PIs		NNRTIs			
		EFV	ETR	NVP	RPV[a]
ATV Unboosted	**PK Data**	EFV: No significant change ATV AUC ↓ 74%	ETR AUC ↑ 50% and C_{min} ↑ 58% ATV AUC ↓ 17% and C_{min} ↓ 47%	↓ ATV possible	↑ RPV possible
	Dose	**Do not coadminister.**	**Do not coadminister.**	**Do not coadminister.**	Standard doses
ATV/c	**PK Data**	↓ ATV possible ↓ COBI possible	↓ ATV possible ↓ COBI possible	↓ ATV possible ↓ COBI possible	↑ RPV possible ↔ ATV expected
	Dose	EFV standard dose In ART-Naive Patients: • ATV 400 mg + COBI 150 mg once daily • **Do not use coformulated ATV/c 300 mg/150 mg.** In ART-Experienced Patients: • **Do not coadminister.**	**Do not coadminister.**	**Do not coadminister.**	Standard doses
ATV/r	**PK Data**	(ATV 400 mg + RTV 100 mg) Once Daily: • ATV concentrations similar to (ATV 300 mg + RTV 100 mg) without EFV	(ATV 300 mg + RTV 100 mg) Once Daily: • ETR AUC and C_{min} both ↑ ~30% • ATV AUC ↔ and C_{min} ↓ 18%	(ATV 300 mg + RTV 100 mg) Once Daily: • ATV AUC ↓ 42% and C_{min} ↓ 72% • NVP AUC ↑ 25%	↑ RPV possible
	Dose	EFV standard dose In ART-Naive Patients: • (ATV 400 mg + RTV 100 mg) once daily In ART-Experienced Patients: • **Do not coadminister.**	ETR standard dose (ATV 300 mg + RTV 100 mg) once daily	**Do not coadminister.**	Standard doses
DRV/c	**PK Data**	↓ DRV possible ↓ COBI possible	↓ DRV possible ↓ COBI possible	↓ DRV possible ↓ COBI possible	↔ DRV expected ↑ RPV possible
	Dose	**Do not coadminister.**	**Do not coadminister.**	**Do not coadminister.**	Standard doses

Table 19a. Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors[a] (Last updated October 17, 2017; last reviewed October 17, 2017) (Page 2 of 2)

PIs		NNRTIs			
		EFV	ETR	NVP	RPV[a]
DRV/r	PK Data	With (DRV 300 mg + RTV 100 mg) BID: • EFV AUC ↑ 21% • DRV AUC ↓ 13% and C_{min} ↓ 31%	ETR 100 mg BID with (DRV 600 mg + RTV 100 mg) BID: • ETR AUC ↓ 37% and C_{min} ↓ 49% • DRV: No significant change	With (DRV 400 mg + RTV 100 mg) BID: • NVP AUC ↑ 27% and C_{min} ↑ 47% • DRV AUC ↑ 24%[b]	RPV 150 mg Once Daily with (DRV 800 mg + RTV 100 mg) Once Daily: • RPV AUC ↑ 130% and C_{min} ↑ 178% • DRV: No significant change
	Dose	Clinical significance unknown. Use standard doses and monitor patient closely. Consider monitoring drug levels.	Standard doses Despite reduced ETR concentration, safety and efficacy of this combination have been established in a clinical trial.	Standard doses	Standard doses
LPV/r	PK Data	With LPV/r Tablets 500/125 mg[c] BID: • LPV concentration similar to that with LPV/r 400/100 mg BID without EFV	With LPV/r Tablets: • ETR AUC ↓ 35% (comparable to the decrease with DRV/r) • LPV AUC ↓ 13%	With LPV/r Capsules: • LPV AUC ↓ 27% and C_{min} ↓51%	RPV 150 mg Once Daily with LPV/r Capsules: • RPV AUC ↑ 52% and C_{min} ↑ 74% • LPV: No significant change
	Dose	LPV/r tablets 500/125 mg[c] BID; LPV/r oral solution 533/133 mg BID EFV standard dose	Standard doses	LPV/r tablets 500/125 mg[c] BID; LPV/r oral solution 533/133 mg BID NVP standard dose	Standard doses
TPV Always use with RTV	PK Data	With (TPV 500 mg + RTV 100 mg) BID: • EFV ↔ • TPV AUC ↓ 31% and C_{min} ↓ 42% With (TPV 750 mg + RTV 200 mg) BID: • EFV and TPV: ↔	With (TPV 500 mg + RTV 200 mg) BID: • ETR AUC ↓ 76% and C_{min} ↓ 82% • TPV AUC ↑ 18% and C_{min} ↑ 24%	With (TPV 250 mg + RTV 200 mg) BID or with (TPV 750 mg + RTV 100 mg) BID: • NVP: ↔ • TPV: ↔ expected	↑ RPV possible
	Dose	Standard doses	**Do not coadminister.**	Standard doses	Standard doses

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

[b] Based on between-study comparison.

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

Key to Symbols:

↑ = increase

↓ = decrease

↔ = no change

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

Table 19b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors (Last updated October 17, 2017; last reviewed October 17, 2017) (page 1 of 3)

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

ARV Drugs by Drug Class		INSTIs		
		DTG	EVG/c	RAL
NNRTIs				
EFV	**PK Data**	With DTG 50 mg Once Daily: • DTG AUC ↓ 57% and C_{min} ↓ 75%	↑ or ↓ EVG, COBI, EFV possible	With RAL 400 mg BID: • RAL AUC ↓ 36% and C_{min} ↓ 21% With RAL 1200 mg Once Daily: • RAL AUC ↓ 14% and C_{min} ↔
	Dose	In Patients Without INSTI Resistance: • DTG 50 mg BID In Patients With Certain INSTI-Associated Resistance[a] or Clinically Suspected INSTI Resistance: **• Consider alternative combination.**	**Do not coadminister.**	Standard doses
ETR	**PK Data**	ETR 200 mg BID + DTG 50 mg Once Daily: • DTG AUC ↓ 71% and C_{min} ↓ 88% ETR 200 mg BID with (DRV 600 mg + RTV 100 mg) BID and DTG 50 mg Once Daily: • DTG AUC ↓ 25% and C_{min} ↓ 37% ETR 200 mg BID with (LPV 400 mg + RTV 100 mg) BID and DTG 50 mg Once Daily: • DTG AUC ↑ 11% and C_{min} ↑ 28%	↑ or ↓ EVG, COBI, ETR possible	ETR 200 mg BID + RAL 400 mg BID: • ETR C_{min} ↑ 17% • RAL C_{min} ↓ 34%
	Dose	**Do not coadminister ETR and DTG without concurrently administering ATV/r, DRV/r, or LPV/r.** In Patients Without INSTI Resistance: • DTG 50 mg once daily with ETR (concurrently with ATV/r, DRV/r, or LPV/r) In Patients With Certain INSTI-Associated Resistance[a] or Clinically Suspected INSTI Resistance: • DTG 50 mg BID with ETR (concurrently with ATV/r, DRV/r, or LPV/r)	**Do not coadminister.**	RAL 400 mg BID **Coadministration with RAL 1200 mg once daily is not recommended.**
NVP	**PK Data**	With DTG 50 mg Once Daily: • DTG AUC ↓ 19% and C_{min} ↓ 34%	↑ or ↓ EVG, COBI, NVP possible	No data
	Dose	Standard doses	**Do not coadminister.**	Standard doses

Table 19b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors (Last updated October 17, 2017; last reviewed October 17, 2017) (page 2 of 3)

ARV Drugs by Drug Class		INSTIs		
		DTG	EVG/c	RAL
NNRTIs, continued				
RPV	**PK Data**	With DTG 50 mg Once Daily: • DTG AUC ↔ and C_{min} ↑ 22% • RPV AUC ↔ and C_{min} ↑ 21%	↑ or ↓ EVG, COBI, RPV possible	• RPV ↔ • RAL C_{min} ↑ 27%
	Dose	Standard doses	**Do not coadminister.**	Standard doses
PIs				
ATV/c	**PK Data**	No data	ATV/c + EVG/c: • No data	No data
	Dose	Standard doses	**Do not coadminister.**	Standard doses
ATV +/- RTV	**PK Data**	Unboosted ATV + DTG 30 mg Once Daily: • DTG AUC ↑ 91% and C_{min} ↑ 180% (ATV 300 mg + RTV 100 mg) Once Daily + DTG 30 mg Once Daily: • DTG AUC ↑ 62% and C_{min} ↑ 121%	↑ or ↓ EVG, COBI, ATV possible	With Unboosted ATV: • RAL AUC ↑ 72% With Unboosted ATV and RAL 1200 mg • RAL AUC ↑ 67% With (ATV 300 mg + RTV 100 mg) Once Daily: • RAL AUC ↑ 41%
	Dose	Standard doses	**Do not coadminister.**	Standard doses
DRV/c	**PK Data**	DTG 50 mg Once Daily and DRV/r Once Daily Switched to DRV/c: • DTG C_{min} ↑ 100%	DRV/c + EVG/c: • ↓ EVG possible	No data
	Dose	Standard doses	**Do not coadminister.**	Standard doses
DRV/r	**PK Data**	(DRV 600 mg + RTV 100 mg) BID with DTG 30 mg Once Daily: • DTG AUC ↓ 22% and C_{min} ↓ 38%	↑ or ↓ EVG, COBI, DRV possible	With (DRV 600 mg + RTV 100 mg) BID: • RAL AUC ↓ 29% and C_{min} ↑ 38%
	Dose	Standard doses	**Do not coadminister.**	Standard doses
LPV/r	**PK Data**	With (LPV 400 mg + RTV 100 mg) BID and DTG 30 mg Once Daily: • DTG: No significant effect	↑ or ↓ EVG, COBI, LPV possible RTV and COBI have similar effects on CYP3A.	↓ RAL ↔ LPV/r
	Dose	Standard doses	**Do not coadminister.**	Standard doses
TPV/r	**PK Data**	With (TPV 500 mg + RTV 200 mg) BID and DTG 50 mg Once Daily: • DTG AUC ↓ 59% and C_{min} ↓ 76%	↑ or ↓ EVG, COBI, TPV possible RTV and COBI have similar effects on CYP3A.	With (TPV 500 mg + RTV 200 mg) BID and RAL 400 mg BID: • RAL AUC ↓ 24% and C_{min} ↓ 55%
	Dose	In Patients Without INSTI Resistance: • DTG 50 mg BID In Patients With Certain INSTI-Associated Resistance[a] 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.**

Table 19b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors (Last updated October 17, 2017; last reviewed October 17, 2017) (page 3 of 3)

[a] Refer to DTG product labeling for details.

Key to Symbols:

↑ = increase

↓ = decrease

↔ = no change

Key to Acronyms: ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BID = twice daily; C_{min} = minimum plasma concentration; COBI = cobicistat; CYP = cytochrome P; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; INSTI = integrase strand transfer inhibitor; LPV = lopinavir; LPV/r = lopinavir/ritonavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PK = pharmacokinetic; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; TPV = tipranavir; TPV/r = tipranavir/ritonavir

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

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination	Serum/ Intracellular Half-Lives	Adverse Events[b]
Abacavir (ABC) *Ziagen* **Note:** Generic available. **Also available as a component of fixed-dose combinations (by trade name and abbreviation)**:	Ziagen: • 300 mg tablet • 20 mg/mL oral solution	Ziagen: • 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% Dosage adjustment for ABC is recommended in patients with hepatic insufficiency (see Appendix B, Table 7).	1.5 hours/12–26 hours	• HSRs: Patients who test positive for HLA-B*5701 are at highest risk. HLA screening should be done before initiation of ABC. • For patients with history of HSR, rechallenge **is not recommended**. • Symptoms of HSR may include fever, rash, nausea, vomiting, diarrhea, abdominal pain, malaise, fatigue, or respiratory symptoms such as sore throat, cough, or shortness of breath. • Some cohort studies suggest increased risk of MI with recent or current use of ABC, but this risk is not substantiated in other studies.
Trizivir (ABC/ZDV/3TC) **Note:** Generic available.	Trizivir: • (ABC 300 mg + ZDV 300 mg + 3TC 150 mg) tablet	Trizivir: • 1 tablet BID			
Epzicom (ABC/3TC) **Note:** Generic available.	Epzicom: • (ABC 600 mg + 3TC 300 mg) tablet	Epzicom: • 1 tablet once daily			
Triumeq (ABC/3TC/DTG)	Triumeq: • (ABC 600 mg + 3TC 300 mg + DTG 50 mg) tablet	Triumeq: • 1 tablet once daily			
Didanosine (ddI) *Videx* *Videx EC* **Note:** Generic available; dose same as Videx or Videx EC.	Videx EC: • 125, 200, 250, and 400 mg capsules Videx: • 10 mg/mL oral solution	Body Weight ≥60 kg: • 400 mg once daily *With TDF:* • 250 mg once daily Body Weight <60 kg: • 250 mg once daily *With TDF:* • 200 mg once daily Take 1/2 hour before or 2 hours after a meal. **Note:** Preferred dosing with oral solution is BID (total daily dose divided into 2 doses).	Renal excretion: 50% Dosage adjustment in patients with renal insufficiency is recommended (see Appendix B, Table 7).	1.5 hours/ >20 hours	• Pancreatitis • Peripheral neuropathy • Retinal changes, optic neuritis • Lactic acidosis with hepatic steatosis with or without pancreatitis (rare but potentially life-threatening toxicity) • Nausea, vomiting • Potential association with noncirrhotic portal hypertension; in some cases, patients presented with esophageal varices • One cohort study suggested increased risk of MI with recent or current use of ddI, but this risk is not substantiated in other studies. • Insulin resistance/diabetes mellitus

Appendix B, Table 1. Characteristics of Nucleoside Reverse Transcriptase Inhibitors (Last updated October 17, 2017; last reviewed October 17, 2017) (page 2 of 6)

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination	Serum/ Intracellular Half-Lives	Adverse Events[b]
Emtricitabine (FTC) *Emtriva* **Also available as a component of fixed-dose combinations (by trade name and abbreviation):**	Emtriva: • 200 mg hard gelatin capsule • 10 mg/mL oral solution	Emtriva *Capsule:* • 200 mg once daily *Oral Solution:* • 240 mg (24 mL) once daily Take without regard to meals.	Renal excretion: 86% Dosage adjustment in patients with renal insufficiency is recommended (see Appendix B, Table 7).	10 hours/>20 hours	• Minimal toxicity • Hyperpigmentation/skin discoloration • Severe acute exacerbation of hepatitis may occur in patients with HBV/HIV coinfection who discontinue FTC.
Atripla (FTC/EFV/TDF)	Atripla: • (FTC 200 mg + EFV 600 mg + TDF 300 mg) tablet	Atripla: • 1 tablet at or before bedtime • Take on an empty stomach to reduce side effects.			
Complera (FTC/RPV/TDF)	Complera: • (FTC 200 mg + RPV 25 mg + TDF 300 mg) tablet	Complera: • 1 tablet once daily with a meal			
Descovy (FTC/TAF)	Descovy: • (FTC 200 mg + TAF 25 mg) tablet	Descovy: • 1 tablet once daily			
Genvoya (FTC/EVG/c/TAF)	Genvoya: • (FTC 200 mg + EVG 150 mg + COBI 150 mg + TAF 10 mg) tablet	Genvoya: • 1 tablet once daily with food			
Odefsey (FTC/RPV/TAF)	Odefsey: • (FTC 200 mg + RPV 25 mg + TAF 25 mg) tablet	Odefsey: • 1 tablet once daily with a meal			
Stribild (FTC/EVG/c/TDF)	Stribild: • (FTC 200 mg + EVG 150 mg + COBI 150 mg + TDF 300 mg) tablet	Stribild: • 1 tablet once daily with food			
Truvada (FTC/TDF)	Truvada: • (FTC 200 mg + TDF 300 mg) tablet	Truvada: • 1 tablet once daily			

Appendix B, Table 1. Characteristics of Nucleoside Reverse Transcriptase Inhibitors (Last updated October 17, 2017; last reviewed October 17, 2017) (page 3 of 6)

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination	Serum/ Intracellular Half-Lives	Adverse Events[b]
Lamivudine (3TC) *Epivir* **Note:** Generic available. **Also available as a component of fixed-dose combinations (by trade name and abbreviation):**	Epivir: • 150 and 300 mg tablets • 10 mg/mL oral solution	Epivir: • 300 mg once daily *or* • 150 mg BID Take without regard to meals.	Renal excretion: 70% Dosage adjustment in patients with renal insufficiency is recommended (see Appendix B, Table 7).	5–7 hours/ 18–22 hours	• Minimal toxicity • Severe acute exacerbation of hepatitis may occur in patients with HBV/HIV coinfection who discontinue 3TC.
Combivir (3TC/ZDV) **Note:** Generic available.	Combivir: • (3TC 150 mg + ZDV 300 mg) tablet	Combivir: • 1 tablet BID			
Epzicom (3TC/ABC) **Note:** Generic available.	Epzicom: • (3TC 300 mg + ABC 600 mg) tablet	Epzicom: • 1 tablet once daily			
Trizivir (3TC/ZDV/ABC) **Note:** Generic available.	Trizivir: • (3TC 150 mg + ZDV 300 mg + ABC 300 mg) tablet	Trizivir: • 1 tablet BID			
Triumeq (3TC/ABC/DTG)	Triumeq: • (3TC 300 mg + ABC 600 mg + DTG 50 mg) tablet	Triumeq: • 1 tablet once daily			
Stavudine (d4T) *Zerit* **Note:** Generic available.	Zerit: • 15, 20, 30, and 40 mg capsules • 1 mg/mL oral solution	Body Weight ≥60 kg: • 40 mg BID Body Weight <60 kg: • 30 mg BID Take without regard to meals. **Note:** WHO recommends 30 mg BID dosing regardless of body weight.	Renal excretion: 50% Dosage adjustment in patients with renal insufficiency is recommended (see Appendix B, Table 7).	1 hour/ 7.5 hours	• Peripheral neuropathy • Lipoatrophy • Pancreatitis • Lactic acidosis/severe hepatomegaly with hepatic steatosis (rare but potentially life-threatening toxicity) • Hyperlipidemia • Insulin resistance/diabetes mellitus • Rapidly progressive ascending neuromuscular weakness (rare)

Appendix B, Table 1. Characteristics of Nucleoside Reverse Transcriptase Inhibitors (Last updated October 17, 2017; last reviewed October 17, 2017) (page 4 of 6)

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination	Serum/ Intracellular Half-Lives	Adverse Events[b]
Tenofovir Alafenamide (TAF) *Vemlidy* **Note:** Available as a 25-mg tablet for the treatment of HBV. **Fixed-dose combinations for HIV are listed below (by trade name and abbreviation):**	See fixed-dose combinations for HIV treatment below.	See fixed-dose combinations for HIV treatment below.	Metabolized by cathepsin A; P-glycoprotein substrate Not recommended in patients with CrCl <30 mL/min.	0.5 hours/ 150–180 hours	• Renal insufficiency, Fanconi syndrome, proximal renal tubulopathy (less likely than from TDF) • Osteomalacia, decrease in bone mineral density (lesser effect than from TDF) • Severe acute exacerbation of hepatitis may occur in patients with HBV/HIV coinfection who discontinue TAF. • Diarrhea, nausea, headache
Descovy (TAF/FTC)	Descovy: • (FTC 200 mg + TAF 25 mg) tablet	Descovy: • 1 tablet once daily			
Genvoya (TAF/EVG/c/FTC)	Genvoya: • (TAF 10 mg + EVG 150 mg + COBI 150mg + FTC 200 mg) tablet	Genvoya: • 1 tablet once daily with food			
Odefsey (TAF/RPV/FTC)	Odefsey: • (TAF 25 mg + RPV 25 mg + FTC 200 mg) tablet	Odefsey: • 1 tablet once daily with a meal			

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

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination	Serum/ Intracellular Half-Lives	Adverse Events[b]
Tenofovir Disoproxil Fumarate (TDF) Viread **Also available as a component of fixed-dose combinations (by trade name and abbreviation):**	Viread: • 150, 200, 250, and 300 mg tablets • 40 mg/g oral powder	Viread: • 300 mg once daily, *or* • 7.5 level scoops once daily (dosing scoop dispensed with each prescription; 1 level scoop contains 1 g of oral powder) • 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). **Do not mix oral powder with liquid.**	Renal excretion is primary route of elimination. Dosage adjustment in patients with renal insufficiency is recommended (see Appendix B, Table 7).	17 hours/ >60 hours	• Renal insufficiency, Fanconi syndrome, proximal renal tubulopathy • Osteomalacia, decrease in bone mineral density • Severe acute exacerbation of hepatitis may occur in patients with HBV/HIV coinfection who discontinue TDF. • Asthenia, headache, diarrhea, nausea, vomiting, and flatulence
Atripla (TDF/EFV/FTC)	Atripla: • (TDF 300 mg + EFV 600 mg + FTC 200 mg) tablet	Atripla: • 1 tablet at or before bedtime • Take on an empty stomach to reduce side effects.			
Complera (TDF/RPV/FTC)	Complera: • (TDF 300 mg + RPV 25 mg + FTC 200 mg) tablet	Complera: • 1 tablet once daily • Take with a meal.			
Stribild (TDF/EVG/c/FTC)	Stribild: • (TDF 300 mg + EVG 150 mg + COBI 150 mg + FTC 200 mg) tablet	Stribild: • 1 tablet once daily • Take with food.			
Truvada (TDF/FTC)	Truvada: • (TDF 300 mg + FTC 200 mg) tablet	Truvada: • 1 tablet once daily • Take without regard to meals.			

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

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination	Serum/ Intracellular Half-Lives	Adverse Events[b]
Zidovudine (ZDV) *Retrovir* **Note:** Generic available. **Also available as a component of fixed-dose combinations (by trade name and abbreviation):**	Retrovir: • 100 mg capsule • 300 mg tablet (only available as generic) • 10 mg/mL intravenous solution • 10 mg/mL oral solution	Retrovir: • 300 mg BID, *or* • 200 mg TID • Take without regard to meals.	Metabolized to GAZT Renal excretion of GAZT Dosage adjustment in patients with renal insufficiency is recommended (see Appendix B, Table 7).	1.1 hours/ 7 hours	• Bone marrow suppression: macrocytic anemia or neutropenia • Nausea, vomiting, headache, insomnia, asthenia • Nail pigmentation • Lactic acidosis/severe hepatomegaly with hepatic steatosis (rare but potentially life-threatening toxicity) • Hyperlipidemia • Insulin resistance/diabetes mellitus • Lipoatrophy • Myopathy
Combivir (ZDV/3TC) **Note:** Generic available.	Combivir: • (ZDV 300 mg + 3TC 150 mg) tablet	Combivir: • 1 tablet BID • Take without regard to meals.			
Trizivir (ZDV/3TC/ABC) **Note:** Generic available.	Trizivir: • (ZDV 300 mg + 3TC 150 mg + ABC 300 mg) tablet	Trizivir: • 1 tablet BID • Take without regard to meals.			

[a] For dosage adjustment in renal or hepatic insufficiency, see Appendix B, Table 7.

[b] Also see Table 14.

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

Appendix B, Table 2. Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors (Last updated October 17, 2017; last reviewed October 17, 2017) (page 1 of 2)

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

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/Metabolic Pathway	Serum Half-Life	Adverse Events[b]
Efavirenz (EFV) *Sustiva* **Also available as a component of a fixed-dose combination (by trade name and abbreviation):**	Sustiva: • 50 and 200 mg capsules • 600 mg tablet	Sustiva: • 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	• Rash[c] • Neuropsychiatric symptoms[d] • Hepatotoxicity • Hyperlipidemia • False-positive results with some cannabinoid and benzodiazepine screening assays reported. • Teratogenic in nonhuman primates • QT interval prolongation
Atripla (EFV/TDF/FTC)	Atripla: • (EFV 600 mg + TDF 300 mg + FTC 200 mg) tablet	Atripla: • 1 tablet once daily, at or before bedtime			
Etravirine (ETR) *Intelence*	• 25, 100, and 200 mg tablets	• 200 mg BID • Take following a meal.	CYP3A4, 2C9, and 2C19 substrate 3A4 inducer; 2C9 and 2C19 inhibitor	41 hours	• Rash, including Stevens-Johnson syndrome[c] • HSRs, characterized by rash, constitutional findings, and sometimes organ dysfunction (including hepatic failure) have been reported. • Nausea

Nevirapine (NVP) *Viramune Viramune XR*
Note: Generic available
	• 200 mg tablet
	• 400 mg XR tablet
	• 50 mg/5 mL oral suspension
		• 200 mg once daily for 14 days (lead-in period); thereafter, 200 mg BID, or 400 mg (Viramune XR tablet) once daily
		• Take without regard to meals.
		• Repeat lead-in period if therapy is discontinued for >7 days.
		• In patients who develop mild-to-moderate rash without constitutional symptoms, continue lead-in period until rash resolves but not longer than 28 days total.
			CYP450 substrate, inducer of 3A4 and 2B6; 80% excreted in urine (glucuronidated metabolites, <5% unchanged); 10% excreted in feces	25–30 hours	• Rash, including Stevens-Johnson syndrome[c]
					• Symptomatic hepatitis, including fatal hepatic necrosis, has been reported:
					  • Rash reported in approximately 50% of cases.
					  • Occurs at a significantly higher frequency in ARV-naive female patients with pre-NVP CD4 counts >250 cells/mm^3 and in ARV-naive male patients with pre-NVP CD4 counts >400 cells/mm^3. NVP should not be initiated in these patients unless the benefit clearly outweighs the risk.

Appendix B, Table 2. Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors (Last updated October 17, 2017; last reviewed October 17, 2017) (page 2 of 2)

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

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/Metabolic Pathway	Serum Half-Life	Adverse Events[b]
Rilpivirine (RPV) *Edurant* **Also available as a component of fixed-dose combinations (by trade name and abbreviation):**	Edurant: • 25 mg tablet	Edurant: • 25 mg once daily • Take with a meal.	CYP3A4 substrate	50 hours	• Rash[c] • Depression, insomnia, headache • Hepatotoxicity • QT interval prolongation
Complera (RPV/TDF/FTC)	Complera: • (RPV 25 mg + TDF 300 mg + FTC 200 mg) tablet	Complera: • 1 tablet once daily • Take with a meal.			
Odefsey (RPV/TAF/FTC)	Odefsey: • (RPV 25 mg + TAF 25 mg + FTC 200 mg) tablet	Odefsey: • 1 tablet once daily • Take with a meal.			

[a] For dosage adjustment in renal or hepatic insufficiency, see Appendix B, Table 7.

[b] Also see Table 14.

[c] Rare cases of Stevens-Johnson syndrome have been reported with most NNRTIs; the highest incidence of rash was seen with NVP.

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

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

Appendix B, Table 3. Characteristics of Protease Inhibitors (Last updated October 17, 2017; last reviewed October 17, 2017) (page 1 of 6)

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

Appendix B, Table 3. Characteristics of Protease Inhibitors (Last updated October 17, 2017; last reviewed October 17, 2017) (page 2 of 6)

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum Half-Life	Storage	Adverse Events[b]
Darunavir (DRV) *Prezista* **Also available as a component of a fixed-dose combination (by trade name and abbreviation):**	• 75, 150, 600, and 800 mg tablets • 100 mg/ mL oral suspension	In ARV-Naive Patients or ARV-Experienced Patients with No DRV Mutations: • (DRV 800 mg + RTV 100 mg) once daily In ARV-Experienced Patients with 1 or More DRV Resistance Mutations: • (DRV 600 mg + RTV 100 mg) BID Unboosted DRV **is not recommended.** Take with food.	CYP3A4 inhibitor and substrate CYP2C9 inducer	15 hours (when combined with RTV)	Room temperature (up to 25° C or 77° F)	• Skin rash (10%): DRV has a sulfonamide moiety; Stevens-Johnson syndrome, toxic epidermal necrolysis, acute generalized exanthematous pustulosis, and erythema multiforme have been reported. • Hepatotoxicity • Diarrhea, nausea • Headache • Hyperlipidemia • Serum transaminase elevation • Hyperglycemia • Fat maldistribution • Increase in serum creatinine (with COBI)
Prezcobix (DRV/c)	Prezcobix: • (DRV 800 mg + COBI 150 mg) tablet	Prezcobix: • 1 tablet once daily • Take with food. **Not recommended** for patients with 1 or more DRV resistance-associated mutations. With TDF: • Not recommended for patients with baseline CrCl <70 mL/min (see Appendix B, Table 7 for the equation for calculating CrCl).	DRV: As above COBI: substrate of CYP3A, CYP2D6 (minor); CYP3A inhibitor			

Appendix B, Table 3. Characteristics of Protease Inhibitors (Last updated October 17, 2017; last reviewed October 17, 2017) (page 3 of 6)

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum Half-Life	Storage	Adverse Events[b]
Fosamprenavir (FPV) *Lexiva* (a prodrug of APV)	• 700 mg tablet • 50 mg/ mL oral suspension	In ARV-Naive Patients: • FPV 1400 mg BID, *or* • (FPV 1400 mg + RTV 100–200 mg) once daily, *or* • (FPV 700 mg + RTV 100 mg) BID In PI-Experienced Patients (Once-Daily Dosing **Not Recommended**): • (FPV 700 mg + RTV 100 mg) BID With EFV: • (FPV 700 mg + RTV 100 mg) BID, *or* • (FPV 1400 mg + RTV 300 mg) once daily *Tablet:* • Without RTV tablet: Take without regard to meals. • With RTV tablet: Take with meals. *Oral Suspension:* • Take without food.	APV is a CYP3A4 substrate, inhibitor, and inducer. Dosage adjustment in patients with hepatic insufficiency is recommended (see Appendix B, Table 7).	7.7 hours (APV)	Room temperature (up to 25° C or 77° F)	• Skin rash (12% to 19%): FPV has a sulfonamide moiety. • Diarrhea, nausea, vomiting • Headache • Hyperlipidemia • Serum transaminase elevation • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia • Nephrolithiasis
Indinavir (IDV) *Crixivan*	• 100, 200, and 400 mg capsules	• 800 mg every 8 hours • Take 1 hour before or 2 hours after meals; may take with skim milk or a low-fat meal. With RTV: • (IDV 800 mg + RTV 100–200 mg) BID • Take without regard to meals.	CYP3A4 inhibitor and substrate Dosage adjustment in patients with hepatic insufficiency is recommended (see Appendix B, Table 7).	1.5–2 hours	Room temperature (15° to 30° C or 59° to 86° F) Protect from moisture.	• Nephrolithiasis • GI intolerance, nausea • Hepatitis • Indirect hyperbilirubinemia • Hyperlipidemia • Headache, asthenia, blurred vision, dizziness, rash, metallic taste, thrombocytopenia, alopecia, and hemolytic anemia • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia

Appendix B, Table 3. Characteristics of Protease Inhibitors (Last updated October 17, 2017; last reviewed October 17, 2017) (page 4 of 6)

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

Appendix B, Table 3. Characteristics of Protease Inhibitors (Last updated October 17, 2017; last reviewed October 17, 2017) (page 5 of 6)

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum Half-Life	Storage	Adverse Events[b]
Ritonavir (RTV) *Norvir* **Also available as a component of a fixed-dose combination (see lopinavir/ ritonavir).**	• 100 mg tablet • 100 mg soft gel capsule • 80 mg/mL oral solution • 100 mg single-packet oral powder Oral solution contains 43% alcohol.	As PK Booster (or Enhancer) for Other PIs: • 100–400 mg per day in 1 or 2 divided doses (refer to other PIs for specific dosing recommendations). *Tablet:* • Take with food. *Capsule and Oral Solution:* • To improve tolerability, take with food if possible.	CYP3A4 > 2D6 substrate; potent 3A4, 2D6 inhibitor; inducer of CYPs 1A2, 2C8, 2C9, and 2C19 and UGT1A1	3–5 hours	Tablets and oral powder do not require refrigeration. Refrigerate capsules. Capsules can be left at room temperature (up to 25° C or 77° F) for up to 30 days. **Oral solution should not be refrigerated.**	• GI intolerance, nausea, vomiting, diarrhea • Paresthesia (circumoral and extremities) • Hyperlipidemia (especially hypertriglyceridemia) • Hepatitis • Asthenia • Taste perversion • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia
Saquinavir (SQV) *Invirase*	• 500 mg tablet • 200 mg capsule	• (SQV 1000 mg + RTV 100 mg) BID Unboosted SQV **is not recommended.** Take with meals or within 2 hours after a meal.	CYP3A4 substrate	1–2 hours	Room temperature (15° to 30° C or 59° to 86° F)	• GI intolerance, nausea, and diarrhea • Headache • Serum transaminase elevation • Hyperlipidemia • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia • PR interval prolongation • QT interval prolongation. Torsades de pointes have been reported. Patients with pre-SQV QT interval >450 msec should not receive SQV.

Appendix B, Table 3. Characteristics of Protease Inhibitors (Last updated October 17, 2017; last reviewed October 17, 2017) (page 6 of 6)

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

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

[b] Also see Table 14.

Key to Acronyms: APV = amprenavir; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; AV = atrioventricular; BID = twice daily; COBI, c = cobicistat; CrCl = creatine clearance; CYP = cytochrome P; DRV = darunavir; DRV/c = darunavir/cobicistat; EFV = efavirenz; FPV = fosamprenavir; GI = gastrointestinal; IDV = indinavir; LPV = lopinavir; LPV/r = lopinavir/ritonavir; msec = millisecond; NFV = nelfinavir; NVP = nevirapine; PI = protease inhibitor; PPI = proton pump inhibitor; RTV = ritonavir; SQV = saquinavir; TDF = tenofovir disoproxil fumarate; TID = three times a day; TPV = tipranavir; TPV/r = tipranavir/ritonavir; UGT = uridine diphosphate glucuronosyltransferase

Appendix B, Table 4. Characteristics of Integrase Inhibitors (Last updated October 17, 2017; last reviewed October 17, 2017) (page 1 of 2)

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathways	Serum Half-Life	Adverse Events[b]
Dolutegravir (DTG) *Tivicay* **Also available as a component of a fixed-dose combination (by trade name and abbreviation):**	• 50 mg tablet	ARV-Naive or ARV-Experienced, INSTI-Naive Patients: • 50 mg once daily ARV-Naive or ARV-Experienced, INSTI-Naive Patients when Coadministered with EFV, FPV/r, TPV/r, or Rifampin: • 50 mg BID INSTI-Experienced Patients with Certain INSTI Mutations (See Product Label) or with Clinically Suspected INSTI Resistance: • 50 mg BID Take without regard to meals.	UGT1A1-mediated glucuronidation Minor contribution from CYP3A4	~14 hours	• HSRs, including rash, constitutional symptoms, and organ dysfunction (including liver injury) have been reported. • Insomnia • Headache • Depression and suicidal ideation (rare; usually in patients with pre-existing psychiatric conditions)
Triumeq (DTG/ABC/3TC)	Triumeq: • (DTG 50 mg + ABC 600 mg + 3TC 300 mg) tablet	Triumeq: • Take 1 tablet daily without regard to meals.			
Elvitegravir (EVG) **Only available as a component of fixed-dose combinations (by trade name and abbreviation):**	See fixed-dose combinations below.	See fixed-dose combinations below.	CYP3A, UGT1A1/3 substrate	~9 hours	• Nausea • Diarrhea • Depression and suicidal ideation (rare; usually in patients with pre-existing psychiatric conditions)
Genvoya (EVG/c/FTC/ TAF)	Genvoya: • (EVG 150 mg + COBI 150 mg + FTC 200 mg + TAF 10 mg) tablet	Genvoya: • 1 tablet once daily with food **Not recommended** for patients with CrCl <30 mL/min (see Appendix B, Table 7 for the equation for calculating CrCl).	EVG: As above COBI: CYP3A, CYP2D6 (minor) substrate; CYP3A inhibitor	~13 hours	
Stribild (EVG/c/FTC/ TDF)	Stribild: • (EVG 150 mg + COBI 150 mg + FTC 200 mg + TDF 300 mg) tablet	Stribild: • 1 tablet once daily with food **Not recommended** for patients with baseline CrCl <70 mL/min (see Appendix B, Table 7 for the equation for calculating CrCl).		~13 hours	

Appendix B, Table 4. Characteristics of Integrase Inhibitors (Last updated October 17, 2017; last reviewed October 17, 2017) (page 2 of 2)

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathways	Serum Half-Life	Adverse Events[b]
Raltegravir (RAL) *Isentress* *Isentress HD*	• 400 mg tablet • 600 mg tablet (HD) • 25 and 100 mg chewable tablets • 100 mg single packet for oral suspension	ARV-Naive Patients or ARV-Experienced Patients: • Isentress: 400 mg BID ARV-Naive or ARV-Experienced Patients who are Virologically Suppressed on a Regimen of RAL 400 mg BID: • Isentress HD: 1200 mg (two 600-mg tablets) once daily With Rifampin: • Isentress: 800 mg BID • Isentress HD: Not recommended Take without regard to meals.	UGT1A1-mediated glucuronidation	~9 hours	• Rash, including Stevens-Johnson syndrome, HSR, and toxic epidermal necrolysis • Nausea • Headache • Diarrhea • Pyrexia • CPK elevation, muscle weakness, and rhabdomyolysis • Insomnia • Depression and suicidal ideation (rare; usually in patients with pre-existing psychiatric conditions)

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

[b] Also see Table 14.

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

Appendix B, Table 5. Characteristics of Fusion Inhibitor (Last updated January 29, 2008; last reviewed October 17, 2017)

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

[a] Also see Table 14.

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

Appendix B, Table 6. Characteristics of CCR5 Antagonist (Last updated March 27, 2012; last reviewed October 17, 2017)

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

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

[b] Also see Table 14.

Key to Acronyms: BID = twice daily; CYP = cytochrome P; EFV = efavirenz; ETR = etravirine; MVC = maraviroc; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; RAL = raltegravir; T20 = enfuvirtide; TPV/r = tipranavir/ritonavir

Appendix B, Table 7. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency (Last updated October 17, 2017; last reviewed October 17, 2017) (page 1 of 6)

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

<table>
<tr><th>Generic Name
(Abbreviation)
Trade Name</th><th>Usual Daily Dose[a]</th><th>Dosing in Renal Insufficiency[b]</th><th>Dosing in Hepatic Impairment</th></tr>
<tr><td colspan="4">NRTIs
Stribild should not be initiated in patients with CrCl <70 mL/min. Use of the following fixed-dose combinations <u>is not recommended</u> in patients with CrCl <50 mL/min: Atripla, Combivir, Complera, Epzicom, Triumeq, or Trizivir. Descovy, Genvoya, Odefsey, and Truvada <u>are not recommended</u> in patients with CrCl <30 mL/min.</td></tr>
<tr><td>Abacavir
(ABC)
Ziagen</td><td>• 300 mg PO BID</td><td>No dosage adjustment necessary</td><td><u>Child-Pugh Class A</u>:
• 200 mg PO BID (use oral solution)
<u>Child-Pugh Class B or C</u>:
• Contraindicated</td></tr>
<tr><td>Didanosine EC
(ddI)
Videx EC</td><td><u>Body Weight ≥60 kg</u>:
• 400 mg PO once daily
<u>Body Weight <60 kg</u>:
• 250 mg PO once daily</td><td><table><tr><th colspan="3">Dose (Once Daily)</th></tr><tr><th>CrCl (mL/min)</th><th>≥60 kg</th><th><60 kg</th></tr><tr><td>30–59</td><td>200 mg</td><td>125 mg</td></tr><tr><td>10–29</td><td>125 mg</td><td>125 mg</td></tr><tr><td><10, HD,[c] CAPD</td><td>125 mg</td><td>75 mg oral solution</td></tr></table></td><td>No dosage adjustment necessary</td></tr>
<tr><td>Didanosine Oral Solution
(ddI)
Videx</td><td><u>Body Weight ≥60 kg</u>:
• 200 mg PO BID, or
• 400 mg PO once daily
<u>Body Weight <60 kg</u>:
• 250 mg PO once daily, or
• 125 mg PO BID</td><td><table><tr><th colspan="3">Dose (Once Daily)</th></tr><tr><th>CrCl (mL/min)</th><th>≥60 kg</th><th><60 kg</th></tr><tr><td>30–59</td><td>200 mg</td><td>150 mg</td></tr><tr><td>10–29</td><td>150 mg</td><td>100 mg</td></tr><tr><td><10, HD,[c] CAPD</td><td>100 mg</td><td>75 mg</td></tr></table></td><td>No dosage adjustment necessary</td></tr>
<tr><td>Emtricitabine
(FTC)
Emtriva</td><td>• 200 mg oral capsule once daily, or
• 240 mg (24 mL) oral solution once daily</td><td><table><tr><th colspan="3">Dose</th></tr><tr><th>CrCl (mL/min)</th><th>Capsule</th><th>Solution</th></tr><tr><td>30–49</td><td>200 mg q48h</td><td>120 mg q24h</td></tr><tr><td>15–29</td><td>200 mg q72h</td><td>80 mg q24h</td></tr><tr><td><15 or on HD[c]</td><td>200 mg q96h</td><td>60 mg q24h</td></tr></table></td><td>No dosage recommendation</td></tr>
<tr><td>Lamivudine
(3TC)
Epivir</td><td>• 300 mg PO once daily, or
• 150 mg PO BID</td><td><table><tr><th>CrCl (mL/min)</th><th>Dose</th></tr><tr><td>30–49</td><td>150 mg q24h</td></tr><tr><td>15–29</td><td>1 x 150 mg, then 100 mg q24h</td></tr><tr><td>5–14</td><td>1 x 150 mg, then 50 mg q24h</td></tr><tr><td><5 or on HD[c]</td><td>1 x 50 mg, then 25 mg q24h</td></tr></table></td><td>No dosage adjustment necessary</td></tr>
<tr><td>Stavudine
(d4T)
Zerit</td><td><u>Body Weight ≥60 kg</u>:
• 40 mg PO BID
<u>Body Weight <60 kg</u>:
• 30 mg PO BID</td><td><table><tr><th colspan="3">Dose</th></tr><tr><th>CrCl (mL/min)</th><th>≥60 kg</th><th><60 kg</th></tr><tr><td>26–50</td><td>20 mg q12h</td><td>15 mg q12h</td></tr><tr><td>10–25 or on HD[c]</td><td>20 mg q24h</td><td>15 mg q24h</td></tr></table></td><td>No dosage recommendation</td></tr>
</table>

Appendix B, Table 7. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency (Last updated October 17, 2017; last reviewed October 17, 2017) (page 2 of 6)

Generic Name (Abbreviation) *Trade Name*	Usual Daily Dose[a]	Dosing in Renal Insufficiency[b]	Dosing in Hepatic Impairment
NRTIs, continued			
Tenofovir Alafenamide/ Emtricitabine (TAF/FTC) *Descovy*	TAF available as a component of fixed-dose combinations for HIV (i.e., Descovy, Genvoya, and Odefsey) • TAF 10 mg PO daily with EVG/c (Genvoya), *or* • TAF 25 mg PO daily in other fixed-dose combinations	**CrCl (ml/min)** / **Dose** <30 or on HD[c] / Not recommended	Child-Pugh Class A or B: • No dosage adjustment Child-Pugh Class C: • No dosage recommendation
Tenofovir Disoproxil Fumarate (TDF) *Viread*	• 300 mg PO once daily	**CrCl (mL/min)** / **Dose** 30–49 / 300 mg q48h 10–29 / 300 mg twice weekly (every 72–96 hours) <10 and not on HD / No recommendation On HD[c] / 300 mg q7d	No dosage adjustment necessary
Tenofovir Disoproxil Fumarate/ Emtricitabine (TDF/FTC) *Truvada*	• 1 tablet PO once daily	**CrCl (mL/min)** / **Dose** 30–49 / 1 tablet q48h <30 or on HD / Not recommended	No dosage recommendation
Zidovudine (ZDV) *Retrovir*	• 300 mg PO BID	**CrCl (mL/min)** / **Dose** <15 or on HD[c] / 100 mg TID or 300 mg once daily	No dosage recommendation
NNRTIs			
Efavirenz (EFV) *Sustiva*	• 600 mg PO once daily, at or before bedtime	No dosage adjustment necessary	Child-Pugh Class A: • No dosage adjustment Child-Pugh Class B or C: • Not recommended
Efavirenz/ Tenofovir Disoproxil Fumarate/ Emtricitabine (EFV/TDF/FTC) *Atripla*	• 1 tablet PO once daily	**Not recommended** for use in patients with CrCl <50 mL/min. Instead, use the individual drugs of the fixed-dose combination and adjust TDF and FTC doses according to CrCl level.	
Etravirine (ETR) *Intelence*	• 200 mg PO BID	No dosage adjustment necessary	Child-Pugh Class A or B: • No dosage adjustment Child-Pugh Class C: • No dosage recommendation
Nevirapine (NVP) *Viramune* *Viramune XR*	• 200 mg PO BID, *or* • 400 mg PO once daily (using Viramune XR formulation)	Patients on HD: • Limited data; no dosage recommendation	Child-Pugh Class A: • No dosage adjustment Child-Pugh Class B or C: • Contraindicated

Appendix B, Table 7. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency (Last updated October 17, 2017; last reviewed October 17, 2017) (page 3 of 6)

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

Appendix B, Table 7. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency (Last updated October 17, 2017; last reviewed October 17, 2017) (page 4 of 6)

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

Appendix B, Table 7. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency (Last updated October 17, 2017; last reviewed October 17, 2017) (page 5 of 6)

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

Appendix B, Table 7. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency (Last updated October 17, 2017; last reviewed October 17, 2017) (page 6 of 6)

[a] Refer to Appendix B, Tables 1–6 for additional dosing information.

[b] Including with chronic ambulatory peritoneal dialysis and hemodialysis.

[c] On dialysis days, take dose after HD session.

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; ATV = atazanavir; ATV/r = atazanavir/ritonavir; AZT = zidovudine; BID = twice daily; COBI, c = cobicistat; CAPD = chronic ambulatory peritoneal dialysis; CrCl = creatinine clearance; CYP = cytochrome P; d4T = stavudine; ddI = didanosine; DRV = darunavir; DTG = dolutegravir; EC = enteric coated; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; FPV = fosamprenavir; FTC = emtricitabine; HD = hemodialysis; IDV = indinavir; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NFV = 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; T20 = 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[a]	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 *or*	<2 mg/dL (<34 µmol/L)	2–3 mg/dL (34 µmol/L to 50 µmol/L)	>3 mg/dL (>50 µmol/L)
Modified total bilirubin[b]	<4 mg/dL	4–7 mg/dL	>7 mg/dL
Prothrombin time (seconds prolonged) *or*	<4	4–6	>6
International normalized ratio (INR)	<1.7	1.7–2.3	>2.3

[a] Encephalopathy Grades

Grade 1: Mild confusion, anxiety, restlessness, fine tremor, slowed coordination

Grade 2: Drowsiness, disorientation, asterixis

Grade 3: Somnolent but rousable, marked confusion, incomprehensible speech, incontinence, hyperventilation

Grade 4: Coma, decerebrate posturing, flaccidity

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

Child-Pugh Classification	Total Child-Pugh Score[a]
Class A	5–6 points
Class B	7–9 points
Class C	>9 points

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