Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents 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 On some occasions, particularly when new information may affect patient safety, unpublished data presented at major conferences or prepared by the FDA and/or manufacturers as warnings to the public may be used as evidence to revise the guidelines.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] (page 1 of 3)

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 if CD4 count is <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							

Table 3. Laboratory Testing Schedule for Monitoring Patients with HIV Before and After Initiation of Antiretroviral Therapy[a] (page 2 of 3)

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]
Tropism Testing		√ If considering a CCR5 antagonist					√ If considering a CCR5 antagonist, or for patients experiencing virologic failure on a 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 Coinfection)	
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, Total Bilirubin	√	√	√	√				√	√ Every 6–12 months
CBC with Differential	√	√	√ If on ZDV	√ If on ZDV or if CD4 testing is done	√			√	√ Every 3–6 months

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

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]
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[p]	√	√						√	

[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 testing every 4 to 8 weeks until viral load is suppressed to <200 copies/mL. Thereafter, repeat testing 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 patients with virologic suppression who are switching therapy because of toxicity or for convenience, viral amplification will not be possible; therefore, resistance testing should not be performed. Results from prior resistance testing can be helpful in constructing a new regimen.

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

[h] If HBsAg, HBsAb, and HBcAb test results are negative, hepatitis B vaccine series should be administered. Refer to the HIV Primary Care Guidelines and the Adult and Adolescent Opportunistic Infections Guidelines for detailed recommendations.[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 the HIV Primary Care Guidelines and the Adult

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
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)**.	Drug-resistance testing can determine whether drug-resistant virus was transmitted. The initial regimen can be modified, if necessary, once resistance test results are available. Genotypic testing is preferred to phenotypic testing because of lower cost, faster turnaround time, and greater sensitivity for detecting mixtures of wild-type and resistant virus.
If ART is deferred, repeat resistance testing may be considered when therapy is initiated **(CIII)**. A genotypic assay is generally preferred **(AIII)**.	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: Drug-resistance testing is recommended at entry into HIV care to guide selection of initial ART **(AII)**. A genotypic assay is generally preferred **(AIII)**.	Transmitted HIV with baseline resistance to at least 1 drug is seen in 10% to 17% of patients, and suboptimal virologic responses may be seen in patients with baseline resistant mutations to ARVs in the prescribed regimen. Some drug-resistance mutations can remain detectable for years in untreated patients with chronic HIV.
For pregnant persons, or if ART will be initiated on the day of or soon after HIV diagnosis, treatment can be initiated prior to receiving resistance testing results.	If necessary, the ART regimen can be modified once resistance test results are available.
If an INSTI is considered for an ART-naive patient **and/or** transmitted INSTI resistance is a concern, providers should supplement standard resistance testing with a specific INSTI genotypic resistance assay, which may need to be ordered separately **(AIII)**.	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.
If therapy is deferred, repeat resistance testing may be considered before initiation of ART **(CIII)**. A genotypic assay is generally preferred **(AIII)**.	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.
If use of a CCR5 antagonist is being considered, a co-receptor tropism assay should be performed **(AI)**.	See Co-Receptor Tropism Assays section.
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)**.	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.
Resistance testing should be done while the patient is taking ART or, if that is not possible, within 4 weeks after ART discontinuation **(AII)**. If >4 weeks have elapsed, resistance testing may still be useful to guide therapy; however, previously-selected mutations can be missed due to lack of drug selective pressure **(CIII)**.	The absence of detectable resistance in such patients must be interpreted with caution when designing subsequent ARV regimens, as mutations may decay with time.
A standard genotypic resistance assay is generally preferred for patients experiencing virologic failure on their first or second regimens and for those with noncomplex resistance patterns **(AII)**.	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.
All prior and current drug-resistance testing results should be reviewed and considered when designing a new regimen for a patient experiencing virologic failure **(AIII)**.	Drug resistance mutations may decay with time, and mutations detected in prior resistance tests may not be detected in current tests, though they remain clinically relevant.
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)**.	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).

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

Clinical Setting and Recommendation	Rationale
Adding phenotypic testing to genotypic testing is generally preferred in patients with known or suspected complex drug-resistance patterns **(BIII)**.	Phenotypic testing can provide additional useful information in patients with complex drug resistance mutation patterns.
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 in suboptimal viral suppression, and it can help the clinician identify the number of active drugs available in the current regimen and assess the need for a new regimen.
In Pregnant Persons with HIV: Genotypic resistance testing is recommended for all pregnant persons before initiation of ART **(AIII)** and for those entering pregnancy with detectable HIV RNA levels while on therapy **(AI)**.	The goals of ART in pregnant persons with HIV are to achieve maximal viral suppression for treatment of maternal HIV and to prevent perinatal transmission of HIV. Genotypic resistance testing will assist the clinician in selecting the optimal regimen for the patient. However, treatment should not be delayed while awaiting results of resistance testing. The initial regimen can be modified once resistance test results are available, if needed.
In Patients with Undetectable Viral Load or Low-Level Viremia: HIV-1 proviral DNA resistance assays may be useful in patients with HIV RNA below the limit of detection or with low-level viremia, where a HIV RNA genotypic assay is unlikely to be successful **(CIII)**.	This test may provide information about previously circulating resistant viral variants that are archived within proviral DNA. These assays may miss some or all prior resistance mutations that have occurred within the viral quasi-species, and therefore they should be interpreted with caution. The clinical utility of HIV-1 proviral DNA assays has not been fully determined.

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

Table 6a. Recommended Antiretroviral Regimens for Initial Therapy (page 1 of 2)

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

Recommended Initial Regimens for Most People with HIV
Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use.
INSTI plus 2 NRTIs: **Note:** For individuals of childbearing potential, see Table 6b before prescribing one of these regimens. • BIC/TAF/FTC **(AI)** • DTG/ABC/3TC[a] **(AI)—if HLA-B*5701 negative** • DTG plus tenofovir[b]/FTC[a] (**AI** for both TAF/FTC and TDF/FTC) • RAL[c] plus tenofovir[b]/FTC[a] (**BI** for TDF/FTC, **BII** 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).
INSTI plus 2 NRTIs: **Note:** For individuals of childbearing potential, see Table 6b before prescribing one of these regimens. • EVG/c/tenofovir[b]/FTC (**BI** for both TAF/FTC and TDF/FTC) • RAL[c] plus ABC/3TC[a] **(CII)—if HLA-B*5701 negative and HIV RNA <100,000 copies/mL** Boosted PI plus 2 NRTIs: (In general, boosted DRV is preferred over boosted ATV) • (DRV/c or DRV/r) plus tenofovir[b]/FTC[a] (AI) • (ATV/c or ATV/r) plus tenofovir[b]/FTCa **(BI)** • (DRV/c or DRV/r) plus ABC/3TC[a] **—if HLA-B*5701 negative (BII)** NNRTI plus 2 NRTIs: • DOR/TDF[b]/3TC **(BI)** or DOR plus TAF[b]/FTC **(BIII)** • EFV plus TDF[b]/FTC[a] (**BI** for EFV 600 mg/TDF/FTC or EFV 600 mg/TDF/3TC, **BII** for EFV 600 mg plus TAF/FTC) • RPV/tenofovir[b]/FTC[a] **(BI)—if HIV RNA <100,000 copies/mL and CD4 cell count >200 cells/mm^3** Regimens to Consider when ABC, TAF, and TDF Cannot be Used or Are Not Optimal: • DTG plus 3TC **(BI)** • DRV/r plus RAL BID **(CI)—if HIV RNA <100,000 copies/mL and CD4 cell count >200 cells/mm^3** • DRV/r once daily plus 3TC[a] **(CI)**
Rating of Recommendations: *A = Strong; B = Moderate; C = Optional* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials, observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies, or regimen comparisons from randomized switch studies; III = Expert opinion*

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

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

[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 RAL 400 mg BID or RAL 1200 mg (two, 600-mg tablets) once daily.

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

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

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

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

Before Initiating DTG:

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

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

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

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

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

This table provides guidance to clinicians in choosing an initial ARV regimen according to various patient and regimen characteristics and specific clinical scenarios. When more than one scenario applies to a person with HIV, clinicians should review considerations for each relevant scenario and use their clinical judgment to select the most appropriate regimen. This table is intended to guide the initial choice of regimen. However, if a person is doing well on a particular regimen, it is not necessary to switch to another regimen based on the scenarios outlined in this table. Please see Table 9 for additional information regarding the advantages and disadvantages of particular ARV medications.

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

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
Pre-ART Characteristics	CD4 cell count <200 cells/mm^3	**Do Not Use the Following Regimens:** • RPV-based regimens • DRV/r plus RAL	A higher rate of virologic failure has been observed in those with low pretreatment CD4 cell counts.
	HIV RNA >100,000 copies/mL	**Do Not Use the Following Regimens:** • RPV-based regimens • ABC/3TC with EFV or ATV/r • DRV/r plus RAL	Higher rates of virologic failure have been observed in those with high pretreatment HIV RNA levels.
	HLA-B*5701 positive or result unknown	**Do not use ABC-containing regimens.**	ABC hypersensitivity, a potentially fatal reaction, is highly associated with the presence of the HLA-B*5701 allele.
	ARV should be started before HIV drug resistance results are available (e.g., in a person with acute HIV) or when rapid initiation of ART is warranted	**Avoid NNRTI-based regimens.** **Avoid ABC.** Recommended ART Regimens: • (DRV/r or DRV/c) plus tenofovir[a]/FTC • DTG plus tenofovir[a]/FTC	Transmitted mutations conferring NNRTI resistance are more likely than mutations associated with PI or INSTI resistance. HLA-B*5701 results may not be available rapidly. Transmitted resistance to DRV and DTG is rare, and these drugs have high barriers to resistance. Refer to Table 6b for further guidance before initiating DTG in persons of childbearing potential.
ART-Specific Characteristics	A 1-pill, once-daily regimen is desired	STR Options as Initial ART Include: • BIC/TAF/FTC • DOR/TDF/3TC • DRV/c/TAF/FTC • DTG/ABC/3TC • EFV/TDF/FTC • EFV/TDF/3TC • EVG/c/TAF/FTC • EVG/c/TDF/FTC • RPV/TAF/FTC • RPV/TDF/FTC	Do not use RPV-based regimens if HIV RNA is >100,000 copies/mL and CD4 cell count is <200/mm^3. Do not use DTG/ABC/3TC if patient is HLA-B*5701 positive. Refer to Table 6b for further guidance before initiating an INSTI in persons of childbearing potential. See Appendix B, Table 10 for ARV dose recommendations in the setting of renal impairment.
	Food effects	Regimens that Can be Taken Without Regard to Food: • BIC-, DOR-, DTG-, or RAL-based regimens	Oral bioavailability of these regimens is not significantly affected by food. Refer to Table 6b for further guidance before initiating an INSTI in persons of childbearing potential.

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

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
ART-Specific Characteristics, continued	Food effects, continued	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 unless the patient has ESRD.** Use ABC or TAF. ABC may be used if patient is HLA-B*5701 negative. If HIV RNA >100,000 copies/mL, do not use ABC/3TC plus (EFV or ATV/r). TAF may be used if CrCl >30 mL/min. Consider avoiding ATV. ART Options When ABC, TAF or TDF Cannot be Used: • DTG plus 3TC • DRV/r plus 3TC • DRV/r plus RAL (if CD4 cell count >200 cells/mm^3 and HIV RNA <100,000 copies/mL)	TDF has been associated with proximal renal tubulopathy. Higher rates of renal dysfunction have been reported in patients using TDF in conjunction with RTV-containing regimens. An adjusted dose of TDF can be used in patients with ESRD or in those who are on hemodialysis. Refer to Appendix B, Table 10 for specific dosing recommendations. 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. Refer to Table 6b for further guidance before initiating an INSTI in persons of childbearing potential.
	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 10 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 patient is HLA-B*5701 negative. If HIV RNA >100,000 copies/mL, do not use ABC/3TC plus (EFV or ATV/r).	TDF is associated with decreases in BMD along with renal tubulopathy, urine phosphate wasting, and resultant osteomalacia. TAF and ABC are associated with smaller declines in BMD than TDF.
	Psychiatric illnesses	**Consider avoiding EFV- and RPV-based regimens.** Patients on INSTI-based regimens who have pre-existing psychiatric conditions should be closely monitored. Some ARVs are contraindicated and some psychiatric medications need dose adjustments when coadministered with certain ARVs.	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. See the drug-drug interaction tables (Tables 21a, 21b, and 21d) for dosing recommendations when drugs used for psychiatric illnesses are used with certain ARVs.

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

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
Presence of Other Conditions, continued	HAD	**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.
	Medication-assisted treatment for opioid dependence	Opioid withdrawal may occur when EFV is initiated in patients who are on a stable dose of methadone. Clinical monitoring is recommended, as medications used to treat opioid dependence may need to be adjusted in some patients.	EFV reduces methadone concentrations and may lead to withdrawal symptoms. See the drug-drug interaction tables (Tables 21a, 21b, and 21d) for dosing recommendations.
	High cardiac risk	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. BIC-, DOR-, DTG-, RAL-, or RPV-based regimens may be considered for those with high cardiac risk.	An increased CV risk with ABC has been observed in some studies. Observational cohort studies reported an association between some PIs (DRV, IDV, FPV, and LPV/r) and an increased risk of CV events; this risk has not been seen with ATV (see text). Further study is needed. BIC-, DOR-, DTG-, RAL- or RPV-based regimens have more favorable lipid profiles than other regimens, although evidence on whether this improves CV outcomes is lacking. Refer to Table 6b for further guidance before initiating an INSTI in persons of childbearing potential.
	Cardiac QTc interval prolongation	Consider avoiding EFV- or RPV-based regimens if patient is taking other medications with known risk of Torsades de Pointes, or in patients at higher risk of Torsades de Pointes.	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 BIC, DOR, DTG, RAL, and RPV have fewer lipid effects.	TDF has been associated with lower lipid levels than ABC or TAF. Refer to Table 6b for further guidance before initiating an INSTI in persons of childbearing potential.
	Patients with history of poor adherence to non-ARV medications or inconsistent engagement in care	Consider using regimens with a boosted PI or DTG. BIC also has a high barrier to resistance, but there is currently no data on its efficacy in this population.	These regimens have a high genetic barrier to resistance. Refer to Table 6b for further guidance before initiating an INSTI in persons of childbearing potential.

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

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
Presence of Other Conditions, continued	Pregnancy	Until more information is available, **do not initiate a DTG-based regimen** for those who are pregnant and within 12 weeks post-conception, because preliminary data suggest that there is an increased risk of NTDs in infants born to those who were receiving DTG at the time of conception.[6,7] Refer to Table 6b and the Perinatal Guidelines for further guidance on ARV use during pregnancy.	
	Patients of childbearing potential who are planning to become pregnant or who are sexually active and not using effective contraception	Until more information is available, **do not initiate a DTG-based regimen in these patients**, because preliminary data suggest that there is an increased risk of NTDs in infants born to those who were receiving DTG at the time of conception.[6,7] Refer to Table 6b for further guidance before initiating an INSTI.	
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 that is 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.	
	Treating TB disease with rifamycins	**TAF and BIC are not recommended with any rifamycin-containing regimen.** If Rifampin is Used: • The following are **not recommended:** PI/c or PI/r, BIC, EVG, DOR, RPV, or TAF. • EFV can be used without dose adjustment. • If RAL is used, increase RAL dose to 800 mg BID. Do **not** use once-daily RAL. • Use DTG at 50 mg BID dose only in patients without selected INSTI mutations (refer to product label).	Rifamycins may significantly reduce TAF and BIC exposures. Rifampin is a strong inducer of CYP3A4 and UGT1A1 enzymes, causing significant decreases in concentrations of PIs, INSTIs, DOR, and RPV. Rifampin has a less significant effect on EFV concentration than on the concentrations of other NNRTIs, PIs, and INSTIs. Refer to Table 6b for further guidance before initiating an INSTI in persons of childbearing potential. See the drug-drug interaction tables (Tables 21a, 21b, 21c, 21d and 21e) and TB/HIV Coinfection for information on ARV use with rifamycins.

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

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

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

	ABC/3TC	TAF/FTC	TDF/FTC	TDF/3TC
Dosing Frequency	Once daily	Once daily	Once daily	Once daily
Available Coformulations for ART-Naive Patients	• ABC/3TC • DTG/ABC/3TC	• TAF 25 mg/FTC • BIC/TAF 25 mg/FTC • DRV/c/TAF 10 mg/FTC • EVG/c/TAF 10 mg/FTC • RPV/TAF 25 mg/FTC	• TDF/FTC • EFV/TDF/FTC • EVG/c/TDF/FTC • RPV/TDF/FTC	• TDF/3TC • DOR/TDF/3TC • EFV 600 mg/TDF/3TC • EFV 400 mg/TDF/3TC
Adverse Effects	ABC: • HSR to ABC is associated with the presence of HLA-B*5701 allele • Increase in CV events is associated with ABC use in some, but not all, cohort studies	TAF: • Renal insufficiency, proximal renal tubulopathy (less frequent than with TDF) • Decrease in BMD (less than with TDF; similar to ABC)	TDF: • Renal insufficiency, proximal renal tubulopathy • Decrease in BMD • Renal and bone toxicity are exacerbated by pharmacologic boosters	TDF: • Renal insufficiency, proximal renal tubulopathy • Decrease in BMD • Renal and bone toxicity are exacerbated by pharmacologic boosters
		FTC: Nail pigmentation		3TC: No significant adverse effects
Other Considerations	• Perform HLA-B*5701 testing before initiating ABC; if result is positive, do not start ABC and add ABC to allergy list • If HIV RNA >100,000 copies/mL, use only with DTG	Also used for HBV treatment. Discontinuation may precipitate flair of HBV. See Appendix B, Table 10 for dose recommendations in patients with renal insufficiency.		

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; BIC= bictegravir; BMD = bone mineral density; CV = cardiovascular; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; HBV = hepatitis B virus; HLA = human leukocyte antigen; HSR = hypersensitivity reaction; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

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

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

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

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

	BIC	DTG	EVG	RAL
Dosing Frequency	Once daily	Once Daily: • In ART-naive or INSTI-naive persons Twice Daily: • If used with certain CYP3A4 and UGT1A1 inducers; *or* • In INSTI-experienced persons with certain INSTI DRMs	Once daily; requires boosting with COBI	• 400 mg BID, *or* • 1200 mg (two 600-mg tablets) once daily
STR Available for ART-Naive Patients	BIC/TAF/FTC	DTG/ABC/3TC	• EVG/c/TAF/FTC • EVG/c/TDF/FTC	No
Available as a Single-Drug Tablet	No	Yes	No	Yes
Approved for ART-Experienced Patients	No	Yes, with BID dosing for patients with some INSTI DRMs	No	Yes, for patients with DRM to PI/r or NNRTIs, but no DRM to INSTIs
Virologic Efficacy Against EVG- or RAL-Resistant HIV	*In vitro* data indicate activity, but no clinical trial data are available	Yes, for some isolates; effective with 50 mg BID dose	No	No
Adverse Effects	Nausea, diarrhea (GI disturbance greater with EVG/c), headache, insomnia. Depression and suicidality are rare, occurring primarily in patients with pre-existing psychiatric conditions.			
	↑ CPK (4%)	Hypersensitivity, hepatotoxicity, ↑ CPK, myositis	↑ TG, ↑ LDL	↑ CPK, myopathy, hypersensitivity, SJS/TEN
CYP3A4 Drug-Drug Interactions	CYP3A4 substrate	CYP3A4 substrate (minor)	EVG is a CYP3A4 substrate; COBI is a CYP3A4 inhibitor	No
Chelation with Polyvalent Cation Supplements and Antacids	Oral absorption of all INSTIs may be reduced by polyvalent cations. See Table 21d for recommendations regarding dosing separation of INSTIs and these drugs.			
Other Key Potential Drug Interactions	UGT1A1 substrate, OCT2 and MATE1 inhibitor	p-gp substrate, UGT1A1 substrate	EVG is a UGT1A1 substrate; COBI is a p-gp inhibitor	UGT1A1 substrate

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; BIC = bictegravir; BID = twice daily; COBI = cobicistat; CPK = creatine phosphokinase; CYP = cytochrome P; DRM = drug resistance mutation; DTG = dolutegravir; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; GI = gastrointestinal; INSTI = integrase strand transfer inhibitor; LDL = low density lipoprotein; MATE = multidrug and toxic compound extrusion; NNRTI = non-nucleoside reverse transcriptase inhibitor; NTD = neural tube defect; OAT = organic anionic transporter; p-gp = p-glycoprotein; PI = protease inhibitor; PI/r = ritonavir-boosted protease inhibitor; RAL = raltegravir; SJS/TEN = Stevens Johnson Syndrome/toxic epidermal necrolysis; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TG = triglyceride; UGT = uridine diphosphate glucuronosyltransferase

Table 8c. Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors that are Recommended for Antiretroviral Therapy-Naive Patients

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

Key to Acronyms: 3TC = lamivudine; CNS = central nervous system; CYP = cytochrome P; DOR = doravirine; EFV = efavirenz; FTC = emtricitabine; H2 = histamine 2; PPI = proton pump inhibitor; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Table 8d. Characteristics of Protease Inhibitor Options that are Recommended for Antiretroviral Therapy-Naive Patients

	ATV	DRV
Dosing Frequency	Once daily	• Once daily for PI-naive patients • Twice daily for PI-experienced patients with certain PI mutations
PK Boosting	PK-boosting with RTV or COBI is generally recommended. Unboosted ATV is also FDA-approved for ART-naive patients.	DRV should only be used with a PK booster (i.e., RTV or COBI).
Fixed-Dose Formulation	• ATV/c	• DRV/c • DRV/c/TAF/FTC
Available as a Single-Drug Tablet	Yes	Yes
Adverse Effects	• Jaundice • Indirect hyperbilirubinemia • Cholelithiasis • Nephrolithiasis • PR prolongation	• Skin rash • Increase in serum transaminases • Hyperlipidemia • A higher cardiovascular risk was reported in participants taking DRV-based regimens than in those taking ATV-based regimens in an observational cohort study.
CYP3A4 Drug-Drug Interactions	CYP3A4 substrate, inhibitor	CYP34A substrate, inhibitor
Other Significant Drug Interactions	ATV absorption is reduced when ATV is given with acid-lowering therapies. See Table 21a for ATV dosing recommendations when the drug is coadministered with acid-lowering agents.	N/A

Key to Acronyms: ART = antiretroviral therapy; ATV = atazanavir; ATV/c = atazanavir/cobicistat; COBI = cobicistat; CYP = cytochrome P; DRV = darunavir; DRV/c = darunavir/cobicistat; FDA = Food and Drug Administration; FTC = emtricitabine; PI = protease inhibitor; PK = pharmacokinetic; RTV = ritonavir; TAF = tenofovir alafenamide

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

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

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
Dual-NRTI	**ABC/3TC**	• Coformulated with DTG • Generic formulations are available for ABC/3TC, ABC, and 3TC.	• May cause life-threatening HSRs in patients who test positive for the HLA-B*5701 allele. As a result, HLA-B*5701 testing is required before use. • 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 BIC, DRV/c, 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 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/3TC	• Coformulated with DOR and EFV
		• Available as the following generic formulations:
		  • TDF
		  • 3TC
		  • TDF/3TC
		  • EFV/TDF/3TC
		• Long-term clinical experience
		• Active against HBV
			• Renal toxicity, including proximal tubulopathy and acute or chronic renal insufficiency, especially when combined with pharmacologic boosters.
			• Osteomalacia has been reported as a consequence of proximal tubulopathy.
			• Decreased BMD has been associated with use of TDF, especially when combined with pharmacologic boosters.

	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 ABC/3TC in patients with baseline viral loads ≥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, especially when combined with pharmacologic boosters. • Osteomalacia has been reported as a consequence of proximal tubulopathy. • Decreased BMD has been associated with use of TDF, especially when combined with pharmacologic boosters.

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

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
INSTI	**BIC**	• Coformulated with TAF/FTC • In trials in ART-naive participants, BIC resistance was not detected • No food requirement	• Compared to other INSTIs, BIC has the shortest post-marketing experience. • Oral absorption of BIC can be reduced by simultaneous administration with drugs or supplements containing polyvalent cations (e.g., Al-, Ca-, or Mg-containing antacids or supplements, or multivitamin tablets with minerals). See dosing recommendations in Table 21d. • Inhibits tubular secretion of creatinine without affecting glomerular function. • CYP3A4 and UGT1A1 substrate (but not a CYP3A4 inducer or inhibitor); potential for drug interactions.
	DTG	• Higher barrier to resistance than EVG or RAL • Coformulated with ABC and 3TC • No food requirement • No CYP3A4 interactions • Favorable lipid profile	• Preliminary data suggests that DTG use before pregnancy and through conception may be associated with an increased risk of NTDs in the infant. See text and Table 6b for recommendations. • Oral absorption of DTG can be reduced by simultaneous administration with drugs containing polyvalent cations (e.g., Al-, Ca-, or Mg-containing antacids or supplements, or multivitamin tablets with minerals). See dosing recommendations in Table 21d. • Inhibits renal tubular secretion of Cr and can increase serum Cr without affecting glomerular function. • UGT1A1 substrate; potential for drug interactions (see Table 21d). • Depression and suicidal ideation (rare; usually in patients with pre-existing psychiatric conditions).
	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 21d. • COBI inhibits active tubular secretion of Cr and can increase serum Cr without affecting renal glomerular function. • Has a lower barrier to resistance than boosted PI-, BIC-, or DTG-based regimens. • Food requirement. • Depression and suicidal ideation (rare; usually in patients with pre-existing psychiatric conditions).

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

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
INSTI, continued	**RAL**	• Compared to other INSTIs, has longest post-marketing experience • No food requirement • No CYP3A4 interactions • Favorable lipid profile	• Has a lower barrier to resistance than boosted PI-, BIC-, or DTG-based regimens. • Increases in creatine kinase, myopathy, and rhabdomyolysis have been reported. • Rare cases of severe HSRs (including SJS and TEN) have been reported. • Higher pill burden than other INSTI-based regimens. • No STR formulation. • Oral absorption of RAL can be reduced by simultaneous administration with drugs containing polyvalent cations (e.g., Al-, Ca-, or Mg-containing antacids or supplements, or multivitamin tablets with minerals). See dosing recommendations in Table 21d. • UGT1A1 substrate; potential for drug interactions (see Table 21d). • Depression and suicidal ideation (rare; usually in patients with pre-existing psychiatric conditions).
NNRTI	**DOR**	• Coformulated with TDF/3TC • Compared to EFV, CNS side effects are less frequent • No food requirement • Favorable lipid profile	• Shorter-term clinical experience than with EFV and RPV. • Potential for CYP450 drug interactions (see Tables 21b, 22a and 22b). • Treatment-emergent DOR resistance mutations may confer resistance to certain NNRTIs.
	EFV	• EFV 600 mg is coformulated with TDF/FTC and TDF/3TC • EFV 400 mg is coformulated with TDF/3TC • EFV 600-mg dose has long-term clinical experience and EFV-based regimens (except for EFV plus ABC/3TC) have well-documented efficacy in patients with high HIV RNA	• Short-and long-term neuropsychiatric (CNS) side effects, including depression and, in some studies, suicidality and catatonia. Screening for depression and suicidality is recommended in people with HIV who are taking a regimen that includes EFV. • Teratogenic in nonhuman primates, although no rate increase has been seen in humans. • Dyslipidemia • Rash • QTc interval prolongation; consider using an alternative to EFV in patients taking medications with known risk of causing Torsades de Pointes or in those at higher risk of Torsades de Pointes. • Transmitted resistance is more common than with PIs and INSTIs. • Greater risk of resistance at the time of treatment failure than with PIs. • Potential for CYP450 drug interactions (see Tables 21b and 22a). • Should be taken on an empty stomach (food increases drug absorption and CNS toxicities).

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

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)

NNRTI, continued	**RPV**	• Coformulated with TDF/FTC and TAF/FTC
		• RPV/TDF/FTC and RPV/TAF/FTC have smaller pill sizes than other coformulated ARV drugs
		• Compared with EFV:
		  • Fewer CNS adverse effects
		  • Fewer lipid effects
		  • Fewer rashes
			• **Not recommended** in patients with pre-ART HIV RNA >100,000 copies/mL or CD4 cell counts <200 cells/mm^3 because of higher rate of virologic failure in these patients.
			• Depression and suicidality
			• QTc interval prolongation; consider using an alternative to RPV in patients taking medications with known risk of causing Torsades de Pointes or in those at higher risk of Torsades de Pointes.
			• Rash
			• Transmitted resistance is more common than with PIs and INSTIs.
			• More NNRTI-, TDF-, and 3TC-associated mutations at virologic failure than with regimens that contain EFV and 2 NRTIs.
			• Potential for CYP450 drug interactions (see Tables 21b and 22a).
			• Meal requirement (>390 kcal)
			• Requires acid for adequate absorption.
			  • **Contraindicated** with PPIs.
			  • Use with H2 antagonists or antacids with caution (see Table 21a for detailed dosing information).

PIs	**ATV/c** or **ATV/r**	• Higher barrier to resistance than NNRTIs, EVG, and RAL • PI resistance at the time of treatment failure is uncommon with PK-enhanced PIs • ATV/c and ATV/r have similar virologic activity and toxicity profiles • Observational cohort studies have found an association between some PIs (DRV, LPV/r, FPV, IDV) and an increased risk of CV events; this risk has not been seen with ATV. Further study is needed. See text for discussion. • Individual ATV and RTV components available as generics	• Commonly causes indirect hyperbilirubinemia, which may manifest as scleral icterus or jaundice. • Food requirement • Absorption depends on food and low gastric pH (see Table 21a for interactions with H2 antagonists, antacids, and PPIs). • Nephrolithiasis, cholelithiasis, nephrotoxicity • GI adverse effects • CYP3A4 inhibitors and substrates: potential for drug interactions (see Table 21a).
	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. • COBI (like RTV) is a potent CYP3A4 inhibitor, which can result in significant interactions with CYP3A substrates.
	DRV/c or **DRV/r**	• Higher barrier to resistance than NNRTIs, EVG, and RAL • PI resistance at the time of treatment failure is uncommon with PK-enhanced PIs	• Skin rash • Food requirement • GI adverse effects • CYP3A4 inhibitors and substrates: potential for drug interactions (see Table 21a). • Increased CV risk reported in one observational cohort study.

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

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
PIs, continued	**DRV/c** (Specific considerations)	• Coformulated as DRV/c and DRV/c/TAF/FTC	• COBI inhibits active tubular secretion of Cr and can increase serum Cr without affecting renal glomerular function. • Coadministration with TDF **is not recommended** in patients with CrCl <70 mL/min. • COBI (like RTV) is a potent CYP3A4 inhibitor, which can result in significant interactions with CYP3A substrates.
	LPV/r	• Only RTV-coformulated PI • No food requirement	• Requires RTV 200 mg per day. • 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 effects. • Possible nephrotoxicity • CYP3A4 inhibitors and substrates: potential for drug interactions (see Table 21a).

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

Table 10. Antiretroviral Components or Regimens Not Recommended as Initial Therapy (page 1 of 3)

ARV Components or Regimens	Reasons for Not Recommending as Initial Therapy
NRTIs	
ABC/3TC/ZDV (Coformulated) As triple-NRTI combination regimen	• Inferior virologic efficacy
ABC/3TC/ZDV plus TDF As quadruple-NRTI combination regimen	• Inferior virologic efficacy
d4T plus 3TC	• Significant toxicities (including lipoatrophy, peripheral neuropathy) and hyperlactatemia (including symptomatic and life-threatening lactic acidosis, hepatic steatosis, and pancreatitis)
ddI plus 3TC (or FTC)	• Inferior virologic efficacy • Limited clinical trial experience in ART-naive patients • ddI toxicities, such as pancreatitis and peripheral neuropathy
ddI plus 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

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

ARV Components or Regimens	Reasons for Not Recommending as Initial Therapy
NRTIs, continued	
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 (3 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	• Higher pill burden than other PI-based regimens • Higher RTV dose than other PI-based regimens • GI intolerance
NFV	• Inferior virologic efficacy • Diarrhea
RTV as sole PI	• High pill burden • GI intolerance • Metabolic toxicity
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
Entry Inhibitors	
T-20 Fusion Inhibitor	• Only studied in patients with virologic failure • Twice-daily subcutaneous injections • High rate of injection site reactions
IBA CD4 Post-Attachment Inhibitor	• Only studied in a very small number of patients with virologic failure • Requires IV therapy • High cost

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

ARV Components or Regimens	Reasons for Not Recommending as Initial Therapy
Entry Inhibitors, continued	
MVC CCR5 Antagonist	• 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 = cobicistat; d4T = stavudine; ddI = didanosine; DLV = delavirdine; DRV = darunavir; ECG = electrocardiogram; EFV = efavirenz; ETR = etravirine; FPV = fosamprenavir; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; GI = gastrointestinal; IBA = ibalizumab; IDV = indinavir; IDV/r = indinavir/ritonavir; IV = intravenous; LPV = lopinavir; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; RTV = ritonavir; SJS = Stevens Johnson Syndrome; SQV = saquinavir; SQV/r = saquinavir/ritonavir; T-20 = enfuvirtide; TDF = tenofovir disoproxil fumarate; TEN = toxic epidermal necrolysis; TPV = tipranavir; TPV/r = tipranavir/ritonavir; ZDV = zidovudine

Table 11. Antiretroviral Options for Patients with Virologic Failure

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

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

Clinical Scenario	Type of Failing Regimen	Resistance Considerations	New Regimen Options[a,b]	Goal
First Regimen Failure	NNRTI plus 2 NRTIs	Most likely resistant to NNRTI +/- 3TC/FTC (i.e., NNRTI mutations +/- M184V/I).[c] Additional NRTI mutations may also be present.	• Boosted PI plus 2 NRTIs (at least 1 active) **(AIII)**; *or* • DTG[d] plus 2 NRTIs (at least 1 active) **(AI)**; *or* • Boosted PI plus INSTI **(AIII)**	Resuppression
	Boosted PI plus 2 NRTIs	Most likely no resistance, or resistance only to 3TC/FTC (i.e., M184V/I, without resistance to other NRTIs)[c]	• Continue same regimen **(AII)**; *or* • Another boosted PI plus 2 NRTIs (at least 1 active) **(AII)**; *or* • INSTI plus 2 NRTIs (at least 1 active; if only 1 of the NRTIs is fully active, or, if adherence is a concern, DTG[d] is preferred over the other INSTIs) **(AIII)**; *or* • Another boosted PI plus INSTI **(BIII)**	Resuppression
	INSTI plus 2 NRTIs	No INSTI resistance (can have 3TC/FTC resistance, i.e., only M184V/I, usually without resistance to other NRTIs)[c]	• Boosted PI plus 2 NRTIs (at least 1 active) **(AIII)**; *or* • DTG[d] plus 2 NRTIs (at least 1 active) **(AIII)**; *or* • Boosted PI plus INSTI **(BIII)**	Resuppression

Table 11. Antiretroviral Options for Patients with Virologic Failure

Clinical Scenario	Type of Failing Regimen	Resistance Considerations	New Regimen Options[a,b]	Goal
First Regimen Failure, continued	INSTI plus 2 NRTIs	EVG or RAL +/- 3TC/FTC resistance Resistance to first-line BIC or DTG is rare	• Boosted PI plus 2 NRTIs (at least 1 active) **(AIII)**; *or* • DTG[d,e] twice daily (if patient is sensitive to DTG) plus 2 active NRTIs (AIII); *or* • DTG[d,e] twice daily (if patient is sensitive to DTG) plus a boosted PI (AIII) • BIC has not been studied in this setting and **cannot be recommended**.	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 when no other options are available • Consider using an ARV with a different mechanism of action	Resuppression
	Multiple or extensive drug resistance with few treatment options	Use past and current genotypic and phenotypic resistance testing to guide therapy Consider viral tropism assay if use of MVC is considered Consult an expert in drug resistance, if needed	• Identify as many active or partially active drugs as possible based on resistance test results • Consider using an 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, keeping viral load as low as possible and CD4 cell count as high as possible
Previously on Treatment, Suspected Drug Resistance, Limited or Incomplete ART and Resistance History	Unknown	Obtain medical records if possible Resistance testing may be helpful in identifying drug resistance mutations, even if the patient has been off ART. Keep in mind that resistance mutations may not be detected in the absence of drug pressure.	• 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 barriers to resistance (e.g., DTG[d,e] and/or boosted DRV)	Resuppression

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

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

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

[d] Preliminary data from Botswana suggested that there is an increased risk of NTDs in infants born to those who were receiving DTG at the time of conception.[47,48] Pregnancy testing should therefore be performed for those of childbearing potential prior to initiation of DTG. Please refer to the discussion at the beginning of this table for further recommendations.

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

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

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

Suspicion of Acute HIV-1 Infection:

- Health care providers should consider the possibility of acute HIV-1 infection in individuals with signs, symptoms, or the laboratory findings described below and recent (within 2 to 6 weeks) high risk of exposure to HIV-1.[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, and 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 that potentially carries HIV-1.
- **Differential Diagnosis:** The differential diagnosis of HIV-1 infection may include but is not limited to viral illnesses such as EBV and non-EBV (e.g., cytomegalovirus) infectious mononucleosis syndromes, influenza, viral hepatitis, streptococcal infection, or syphilis.

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 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 this case, the diagnosis of HIV-1 infection should be later confirmed by subsequent documentation of HIV-1 antibody seroconversion.

Antiretroviral Therapy After Diagnosis of Early HIV-1 Infection:

- ART is recommended for all individuals with HIV-1 **(AI)** and should be offered to all patients with early HIV-1 infection.
- A pregnancy test should be performed for all individuals who receive a diagnosis of early HIV infection and who are of childbearing potential **(AIII)**.
- Pregnant patients with early HIV-1 infection should begin ART as soon as possible for their own health and to prevent perinatal transmission of HIV-1 **(AI)**.
- A blood sample for genotypic drug resistance testing should be obtained before initiation of ART to guide the selection of the regimen **(AII)**, but ART should be initiated as soon as possible, often 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)**.
- Preliminary data from Botswana suggested that infants born to women who were receiving DTG at the time of conception have an increased risk of neural tube defects. Until more information is available, DTG **should not be prescribed** for individuals:
  - Who are pregnant and within 12 weeks post-conception **(AII)**;
  - Who are of childbearing potential, who are sexually active, and who are not using effective contraception **(AII)**; *or*
  - Who are contemplating pregnancy **(AII)**.
- 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)**.
- Once initiated, the goal of ART should be sustained plasma virologic suppression, and ART should be continued indefinitely **(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: Ag/Ab = antigen/antibody; ART = antiretroviral therapy; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EBV = Epstein-Barr virus; FTC = emtricitabine; INSTI = integrase strand transfer inhibitor; PI = protease inhibitor; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Table 13. Medications for Treatment of Substance Use Disorders

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

Key: ARV = antiretroviral; CrCl = creatinine clearance; CYP = cytochrome P; FDA = Food and Drug Administration; FPV = fosamprenavir; LPV/r = lopinavir/ritonavir; OUD = opioid use disorder; OTP = opioid treatment program; PO = orally; RTV = ritonavir; SR = sustained release

Table 14. Potential Interactions Between the Drugs Used in Gender-Affirming Hormone Therapy and Antiretroviral Drugs

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

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

Key: ARV = antiretroviral; BIC = bictegravir; DOR = doravirine; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; GAHT = gender-affirming hormone therapy; IBA = ibalizumab; INSTI = integrase strand transfer inhibitor; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; RAL = raltegravir; RPV = rilpivirine; T-20 = enfuvirtide

Table 15. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of HCV in Adults with HIV (page 1 of 4)

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

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

Selected HIV Drugs	HCV Direct-Acting Antiviral Agents								
			Coformulated						
					SHOULD NOT BE USED IN THOSE WITH MODERATE TO SEVERE HEPATIC IMPAIRMENT (Cirrhosis classified as Child-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 15. 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								
			Coformulated						
					SHOULD NOT BE USED IN THOSE WITH MODERATE TO SEVERE HEPATIC IMPAIRMENT (Cirrhosis classified as Child-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
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									
DOR	✓	✓	✓ If used with TDF, monitor for TDF toxicity.	✓	✓	✓	✓	✓	✓
EFV	✓ ↑ DCV dose to 90 mg/day	✓		✘	✘	✘	✘	✘	✘
ETR	✓ ↑ DCV dose to 90 mg/day	✓		✘	✘	✘	✘	✘	✘

Table 15. 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								
			Coformulated						
					SHOULD NOT BE USED IN THOSE WITH MODERATE TO SEVERE HEPATIC IMPAIRMENT (Cirrhosis classified as Child-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
NNRTIs, continued									
NVP	✓ ↑ DCV dose to 90 mg/day	✓	✓ If used with TDF, monitor for TDF toxicity.	✘	✘	✘	✘	✘	✘
RPV	✓	✓		✓	✓	✓	✓	✘	✓
INSTIs									
BIC/TAF/FTC	✓	✓	✓	✓	✓	✓	✓	✓	✓
DTG	✓	✓	✓ If used with TDF, monitor for TDF toxicity.	✓	✓	✓	✓	✓	✓
EVG/c/TDF/ FTC	✓ ↓ DCV dose to 30 mg/day	✓	✘	✓ If used with TDF, monitor for TDF toxicity.	✓ If used with TDF, monitor for TDF toxicity. Consider monitoring for hepatotoxicity.[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	✓	✓	✓	✓	✓	✓	✓	✘	✓

Table 15. 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)

[a] Dasabuvir must be prescribed with ombitasvir/paritaprevir/RTV.

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

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

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

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

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

Key to Symbols:

✓ = ARV agents that can be used concomitantly

✘ = ARV agents not recommended

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

↑ = increase

↓ = decrease

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; COBI = cobicistat; DAA = direct-acting antiviral agents; DCV = daclatasvir; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; DSV = dasabuvir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; FDA = Food and Drug Administration; EVG/c = elvitegravir/cobicistat; FPV = fosamprenavir; FTC = emtricitabine; HCV = hepatitis C virus; IDV = indinavir; INSTI = integrase strand transfer inhibitor; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; PK = pharmacokinetic; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQV = saquinavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV/r = tipranavir/ritonavir

Table 16. 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 16. 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 17. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy (page 1 of 5)

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

Adverse Effect	Drug Class				
	NRTIs	NNRTIs	PIs	INSTIs	EIs
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 the use of vitamin E supplements.	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: Associated with smaller declines in BMD than those seen 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 the use of 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 17. 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	IBA: 8% of patients reported diarrhea in a study of 40 people.
Hepatic Effects	**Reported with most NRTIs.** ZDV, d4T, and 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: Most cases relate to an increase in transaminases. Fulminant hepatitis leading to death or hepatic failure requiring transplantation have been reported. NVP: Severe hepatotoxicity associated with skin rash or hypersensitivity. A 2-week NVP dose escalation may reduce risk. Risk is greater for women with pre-NVP CD4 counts >250 cells/mm^3 and men with pre-NVP CD4 counts >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 and ATV: Jaundice due to indirect hyperbilirubinemia	N/A	MVC: Hepatotoxicity with or without rash or HSRs reported.

Table 17. 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 patient is 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 counts >250 cells/mm^3 and men with pre-NVP CD4 counts >400 cells/mm^3. Overall, risk is higher for women than men. A 2-week dose escalation of NVP reduces risk.	N/A	RAL: HSR reported when RAL is given with other drugs also known to cause HSRs. 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
Lipodystrophy	Lipoatrophy: d4T > ZDV. More likely when NRTIs are coadministered with EFV than with an RTV-boosted PI.	Lipohypertrophy: Trunk fat increase observed with EFV-, PI-, and RAL-containing regimens; however, causal relationship has not been established.			N/A

Table 17. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy (page 4 of 5)

Adverse Effect	Drug Class				
	NRTIs	NNRTIs	PIs	INSTIs	EIs
Myopathy/ Elevated Creatine Phosphokinase	ZDV: Myopathy	N/A	N/A	RAL and 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)	Neuropsychiatric Events: EFV > RPV, DOR > ETR EFV: Somnolence, insomnia, abnormal dreams, dizziness, impaired concentration, depression, psychosis, and suicidal ideation. Symptoms usually subside or diminish after 2–4 weeks. Bedtime dosing may reduce symptoms. Risk factors include presence of psychiatric illness, concomitant use of agents with neuropsychiatric effects, and increased EFV concentrations because of genetic factors or increased absorption with food. An association between EFV and suicidal ideation, suicide, and attempted suicide was found in a retrospective analysis of comparative trials. RPV: Depression, suicidality, sleep disturbances DOR: Sleep disorders and disturbances, dizziness, altered sensorium; depression and suicidality/self-harm	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, and TPV	All INSTIs	MVC, IBA

Table 17. 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: Associated with 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, COBI (as a Boosting Agent for EVG), and BIC: Inhibits Cr secretion without reducing renal glomerular function	IBA: SCr abnormalities ≥Grade 3 reported in 10% of trial participants.
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 Acronyms: 3TC = lamivudine; ABC = abacavir; ART= antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/r = atazanavir/ritonavir; BIC = bictegravir; BMD = bone mineral density; CD4 = CD4 T lymphocyte; Cr = creatinine; CNS = central nervous system; COBI = cobicistat; CPK = creatine phosphokinase; CVD = cardiovascular disease; d4T = stavudine; ddI = didanosine; DLV = delavirdine; DOR = doravirine; DRV = darunavir; DRV/r = darunavir/ritonavir; DTG = dolutegravir; ECG = electrocardiogram; EFV = efavirenz; EI = entry inhibitor; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FPV = fosamprenavir; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; GI = gastrointestinal; HBV = hepatitis B virus; HDL = high-density lipoprotein; HSR = hypersensitivity reaction; IBA = ibalizumab; IDV = indinavir; INSTI = integrase strand transfer inhibitor; LDL = low-density lipoprotein; LPV/r = lopinavir/ritonavir; MI = myocardial infarction; MVC = maraviroc; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SCr = serum creatinine; SQV = saquinavir; SQV/r = saquinavir/ritonavir; TAF = tenofovir alafenamide; TC = total cholesterol; TDF = tenofovir disoproxil fumarate; TG = triglycerides; TPV = tipranavir; TPV/r = tipranavir/ritonavir; ZDV = zidovudine

Table 18. 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]	TAF or ABC[b] 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, or 3TC	ABC use has been associated with CV disease and cardiac events in some, but not all, observational studies. TDF has been associated with lower lipid levels than TAF.
	RTV- or COBI-boosted PI regimens, EFV, EVG/c	RAL, DTG, BIC, or RPV	RAL, DTG, BIC, and RPV have less effect on lipids than RTV- or COBI-boosted PI regimens, EFV, and EVG/c. Large observation cohorts have found an association between some PIs (DRV, FPV, IDV, LPV/r) and an increased risk of CV events. However, this association has not been seen with ATV. Further study is needed.
Central Nervous System, Neuropsychiatric Side Effects Dizziness, suicidal ideation, abnormal dreams, depression	EFV, RPV	ETR, PI/c, or PI/r INSTIs may be used, but monitoring is recommended (see Comments column).	In most patients, EFV-related CNS effects subside within 4 weeks after initiation of the drug. Persistent or intolerable effects should prompt substitution of EFV. INSTIs are associated with insomnia. Depression and suicidality have been infrequently reported with INSTI use, primarily in patients with pre-existing psychiatric conditions.
Dyslipidemia Hypertriglyceridemia (with or without elevated LDL level)	RTV- or COBI-boosted regimens, and EFV	RAL, DTG, BIC, or RPV	Elevated TG and LDL levels are more common with LPV/r and FPV/r than with other RTV-boosted PIs. Improvements in TG and LDL levels have been observed with switch from LPV/r to ATV or ATV/r.[c]

Table 18. 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, BIC, or EVG/c	GI intolerance is common with boosted PIs and is linked to the total dose of RTV. More GI toxicity is seen with LPV/r than with ATV/r or DRV/r. GI effects are often transient and do not warrant substitution unless they are persistent and intolerable.
	Other RTV- or COBI-boosted regimens	RAL, DTG, BIC, or 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, NNRTI	Results of switch studies have been inconsistent. Studies in HIV-negative patients suggest a direct causal effect of LPV/r (and IDV) on insulin resistance. However, traditional risk factors may be stronger risk factors for insulin resistance than the use of any PI.
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 associated with prior thymidine analog (d4T and ZDV) use. Switching from these ARVs prevents worsening lipoatrophy, but fat recovery is typically slow (may take years) and incomplete.
Lipohypertrophy	Accumulation of visceral, truncal, dorsocervical, and breast fat has been observed during ART, particularly during use of older PI-based regimens (e.g., IDV), but whether ART directly causes fat accumulation remains unclear. There is no clinical evidence that switching to another first line regimen will reverse weight or visceral fat gain.		
Rash	NNRTIs (especially NVP and EFV)	PI- or INSTI-based regimen	Mild rashes that develop after initiation of NNRTIs other than NVP rarely require treatment switch. When serious rash develops due to any NNRTI, switch to another drug class.
	DRV/c, DRV/r	ATV/c, ATV/r, or another drug class (e.g., INSTI)	Mild rashes following DRV/r use may resolve without modification of therapy. For more severe reactions, change to an alternative boosted PI or an agent from another drug class.

Table 18. 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] 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, BIC, RAL, or NNRTI	COBI, DTG, BIC, and, to a lesser extent, RPV, can increase SCr through inhibition of creatinine secretion. This effect does not affect glomerular filtration. However, assess patient for renal dysfunction if SCr increases by >0.4 mg/dL.
Stones Nephrolithiasis and cholelithiasis	ATV, ATV/c, ATV/r	DRV/c, DRV/r, INSTI, or NNRTI	This switch should be made if the clinician believes ATV is the cause of the stones.

[a] In patients with chronic active HBV infection, another agent that is 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.

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; BMD = bone mineral density; CD4 = CD4 T lymphocyte; CNS = central nervous system; COBI = cobicistat; CrCl = creatine clearance; CV = cardiovascular; d4T = stavudine; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FPV = fosamprenavir; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; GI = gastrointestinal; HBV = hepatitis B virus; HSR = hypersensitivity reaction; IDV = indinavir; INSTI = integrase strand transfer inhibitor; LDL = low-density lipoprotein; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SCr = serum creatinine; TAF = tenofovir alafenamide; TC = total cholesterol; TDF = tenofovir disoproxil fumarate; TG = triglycerides; ZDV = zidovudine

Table 19. Monthly Average Prices of Commonly Used Antiretroviral Drugs (Last updated November 26, 2018; last reviewed October 25, 2018) (page 1 of 5)

Prescription drug pricing in the United States involves complex systems of negotiations, rebates, discounts, and reimbursement rates. Much of the information used to determine drug prices is confidential, and prices can vary depending on the purchaser, the type of public or private insurance coverage in use, and the number of generic competitors. In addition, price increases that exceed rates of inflation can trigger additional rebates for Medicaid and 340B Drug Discount Program entities. Table 19 includes three benchmark prices, rounded to the nearest dollar, for commonly used antiretroviral (ARV) drugs[a] as a general reference for health care providers when considering the cost of HIV treatment. Health care providers should contact patients' pharmacies or payors regarding actual prices, comparative cost savings, and related formulary restrictions.

Wholesale acquisition cost (WAC) is the list price published by manufacturers for prescription drugs or biologics sold to wholesalers. The WAC price approximates what retail pharmacies pay wholesalers for single-source (e.g., brand-name) drugs. There is a range of WAC prices for generic ARVs, as these are multiple-source products with variable list prices. With increasing competition, actual transactional prices of generic drugs among wholesalers and pharmacies decrease substantially. **Average wholesale price (AWP)** has historically been used as the basis for setting public (e.g., Medicaid) and private (e.g., commercial insurer) reimbursement rates for pharmacies. Neither WAC nor AWP include variable price concessions along supply and payment chains, including discounts and rebates to wholesalers, pharmacies, federal purchasers (e.g., the Veterans' Administration), pharmacy benefit managers, commercial insurers, Medicaid, 340B pharmacies, and AIDS Drug Assistance Programs. The availability of these discounts and rebates depends on product demand, market competition, and WAC price increases set by manufacturers.

Maximum prices are assigned to generic products with three or more therapeutically and pharmaceutically equivalent products, as determined by the Food and Drug Administration. This federally established price is the **federal upper limit (FUL)**. Federal Medicaid will reimburse state Medicaid programs up to this limit for multiple-source drugs (plus the dispensing fee); commercial insurers set their own reimbursement upper limits with pharmacies. Whereas WACs and AWPs are generally set annually, FULs are adjusted monthly, particularly for multiple-source drugs with fluctuating pharmacy acquisition costs. In the table below, the FUL for a drug is described as "pending" if a generic drug currently lacks the competition required to trigger a FUL.

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

Table 19. Monthly Average Prices of Commonly Used Antiretroviral Drugs (Last updated November 26, 2018; last reviewed October 25, 2018) (page 2 of 5)

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

Table 19. Monthly Average Prices of Commonly Used Antiretroviral Drugs (Last updated November 26, 2018; last reviewed October 25, 2018) (page 3 of 5)

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

Table 19. Monthly Average Prices of Commonly Used Antiretroviral Drugs (Last updated November 26, 2018; last reviewed October 25, 2018) (page 4 of 5)

ARV Drug (Generic and Brand Names)	Strength, Formulation	Tablets, Capsules, or mLs per Month	WAC (Monthly)[b]	AWP (Monthly)[b]	FUL (As of 9/1/2018)[c]
Integrase Strand Transfer Inhibitors (INSTIs)					
Dolutegravir					
• Tivicay	50 mg tablet	30 tablets	$1,658	$1,989	N/A
• Tivicay	50 mg tablet	60 tablets	$3,315	$3,978	N/A
Raltegravir					
• Isentress	400 mg tablet	60 tablets	$1,500	$1,800	N/A
• Isentress HD	600 mg tablet	60 tablets	$1,500	$1,800	N/A
Fusion Inhibitor					
Enfuvirtide					
• Fuzeon	90 mg injection kit	60 doses (1 kit)	$3,586	$4,303	N/A
CCR5 Antagonist					
Maraviroc					
• Selzentry	150 mg tablet	60 tablets	$1,511	$1,813	N/A
• Selzentry	300 mg tablet	60 tablets	$1,511	$1,813	N/A
• Selzentry	300 mg tablet	120 tablets	$3,022	$3,626	N/A
CD4-Directed Post-Attachment Inhibitor					
Ibalizumab-uiyk					
• Trogarzo	200 mg vials	8 vials	$9,080	$10,896	N/A
Coformulated Combination Products as Single Tablet Regimens					
Bictegravir/Tenofovir Alafenamide/Emtricitabine					
• Biktarvy	50 mg/25 mg/200 mg	30 tablets	$2,946	$3,535	N/A
Darunavir/Cobicistat/Tenofovir Alafenamide/Emtricitabine					
• Symtuza	600 mg/150 mg/10 mg/200 mg	30 tablets	$3,482	$4,178	N/A
Dolutegravir/Abacavir/Lamivudine					
• Triumeq	50 mg/600 mg/300 mg tablet	30 tablets	$2,805	$3,366	N/A
Dolutegravir/Rilpivirine					
• Juluca	50 mg/25 mg	30 tablets	$2,579	$3,095	N/A
Doravirine/Tenofovir Disoproxil Fumarate/Lamivudine					
• Delstrigo	100 mg/300 mg/300 mg	30 tablets	$2,100	$2,520	N/A

Table 19. Monthly Average Prices of Commonly Used Antiretroviral Drugs (Last updated November 26, 2018; last reviewed October 25, 2018) (page 5 of 5)

ARV Drug (Generic and Brand Names)	Strength, Formulation	Tablets, Capsules, or mLs per Month	WAC (Monthly)[b]	AWP (Monthly)[b]	FUL (As of 9/1/2018)[c]
Coformulated Combination Products as Single Tablet Regimens, continued					
Efavirenz/Tenofovir Disoproxil Fumarate/Emtricitabine					
• Atripla	600 mg/300 mg/200 mg tablet	30 tablets	$2,724	$3,269	N/A
Efavirenz/Tenofovir Disoproxil Fumarate/Lamivudine					
• Symfi	600 mg/300 mg/300 mg tablet	30 tablets	$1,634	$1,961	N/A
• Symfi Lo	400 mg/300 mg/300 mg tablet	30 tablets	$1,634	$1,961	N/A
Elvitegravir/Cobicistat/Tenofovir Alafenamide/Emtricitabine					
• Genvoya	150 mg/150 mg/10 mg/200 mg tablet	30 tablets	$2,946	$3,535	N/A
Elvitegravir/Cobicistat/Tenofovir Disoproxil Fumarate/ Emtricitabine					
• Stribild	150 mg/150 mg/300 mg/200 mg tablet	30 tablets	$3,090	$3,708	N/A
Rilpivirine/Tenofovir Alafenamide/Emtricitabine					
• Odefsey	25 mg/25 mg/200 mg tablet	30 tablets	$2,681	$3,217	N/A
Rilpivirine/Tenofovir Disoproxil Fumarate/Emtricitabine					
• Complera	25 mg/300 mg/200 mg tablet	30 tablets	$2,681	$3,217	N/A
Pharmacokinetic Enhancers (Boosters)					
Cobicistat					
• Tybost	150 mg tablet	30 tablets	$219	$264	N/A
Ritonavir					
• Generic	100 mg tablet	30 tablets	$222	$278	Pending
• Norvir	100 mg tablet	30 tablets	$257	$309	

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

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

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

Table 20. Mechanisms of Antiretroviral-Associated Drug Interactions (Last updated October 25, 2018; last reviewed October 25, 2018) (page 1 of 2)

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

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

ARV Drugs by Drug Class	Mechanisms That May Affect Oral Absorption of ARV Drugs			Enzymes That Metabolize or are Induced or Inhibited by ARV Drugs				Other Mechanisms of Known Drug Interactions
	Increasing Gastric pH	Cationic Chelation	P-glyco-protein	CYP Substrate	CYP Inhibitor	CYP Inducer	UGT1A1	
INSTIs								
BIC	N/A	Concentration decreased by products that contain polyvalent cations (e.g., Ca, Mg, Al, Fe, Zn)	Substrate	3A4	N/A	N/A	Substrate	Inhibitor of renal transporters OCT2 and MATE1
DTG	N/A		Substrate	3A4 (minor)	N/A	N/A	Substrate	Inhibitor of renal transporters OCT2 and MATE1
EVG	N/A		N/A	3A4	N/A	2C9	Substrate	N/A
RAL	N/A		N/A	N/A	N/A	N/A	Substrate	N/A
PK Enhancers (Boosters)								
COBI	N/A	N/A	Inhibitor	3A4	3A4, 2D6	N/A	N/A	N/A
RTV	N/A	N/A	Substrate, inhibitor	3A4, 2D6	3A4, 2D6	1A2, 2B6, 2C8, 2C9, 2C19	Inducer	N/A
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	N/A	Substrate, inducer, inhibitor	3A4	3A4	N/A	Inhibitor	OATP inhibitor
DRV	N/A	N/A	Substrate, inducer	3A4	3A4	2C9	N/A	OATP inhibitor
FPV	Concentration decreased by H2 antagonist	N/A	Substrate, inhibitor	3A4	3A4	N/A	N/A	N/A
LPV	N/A	N/A	Substrate	3A4	3A4	N/A	N/A	OATP inhibitor
SQV	N/A	N/A	Substrate, inhibitor	3A4	3A4	N/A	N/A	OATP inhibitor
TPV	N/A	N/A	Substrate, inducer	3A4	2D6	3A4, 1A2, 2C19	N/A	OATP inhibitor
NNRTIs								
DOR	N/A	N/A	N/A	3A4, 3A5	N/A	N/A	N/A	N/A
EFV	N/A	N/A	N/A	2B6 (primary), 2A6, 3A4	3A4	3A4, 2B6, 2C19	N/A	N/A

Table 20. Mechanisms of Antiretroviral-Associated Drug Interactions (Last updated October 25, 2018; last reviewed October 25, 2018) (page 2 of 2)

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

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

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 1 of 19)

This table provides known or predicted information regarding PK interactions between PIs and non-ARV drugs. When information is available, interactions for PK-boosted (with either RTV or COBI) and unboosted ATV are listed separately. The term "All PIs" refers to both unboosted ATV and PIs boosted with either RTV or COBI, except the PIs noted below. For interactions between ARV agents and for dosing recommendations, refer to Tables 21c, 22a, and 22b.

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

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

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia			
Alfuzosin	All PIs	↑ alfuzosin expected	**Contraindicated.**
Doxazosin	All PIs	↑ doxazosin possible	Initiate doxazosin at lowest dose and titrate while monitoring for clinical response/toxicity. Dose reduction may be necessary.
Tamsulosin	All PIs	↑ tamsulosin expected	**Coadministration is not recommended.** If coadministered, monitor for tamsulosin toxicities.
Terazosin	All PIs	↔ or ↑ terazosin possible	Initiate terazosin at lowest dose and titrate while monitoring for clinical response/toxicity. Dose reduction may be necessary.
Silodosin	All PIs	↑ silodosin expected	**Contraindicated.**
Acid Reducers			
Antacids	ATV, ATV/c, ATV/r	When given simultaneously, ↓ ATV expected	Give ATV at least 2 hours before or 1–2 hours after antacids or buffered medications.
	TPV/r	TPV AUC ↓ 27%	Give TPV at least 2 hours before or 1 hour after antacids.
H2 Receptor Antagonists	ATV (unboosted)	↓ ATV	H2 receptor antagonist single dose should not exceed a dose equivalent to famotidine 20 mg, and the total daily dose should not exceed a dose equivalent to famotidine 20 mg BID in PI-naive patients. Unboosted ATV plus famotidine should not be used in combination in PI-experienced patients. Give ATV at least 2 hours before and at least 10 hours after the H2 receptor antagonist.
	ATV/c, ATV/r	↓ ATV	H2 receptor antagonist dose should not exceed a dose equivalent to famotidine 40 mg BID in ART-naive patients or famotidine 20 mg BID in ART-experienced patients. Give ATV 300 mg plus (COBI 150 mg **or** RTV 100 mg) simultaneously with and/or ≥10 hours after the dose of H2 receptor antagonist. If using TDF and H2 receptor antagonist in ART-experienced patients, use ATV 400 mg plus (COBI 150 mg **or** RTV 100 mg).
	DRV/c, DRV/r, LPV/r	↔ demonstrated or expected	No dose adjustment necessary.

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 2 of 19)

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers, continued			
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 dose to no more than omeprazole 40 mg daily.
	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** in patients who require apixaban 2.5 mg twice daily. In patients who require apixaban 5 mg or 10 mg twice daily, reduce apixaban dose by 50%.
Betrixaban	ATV/c, ATV/r, LPV/r	↑ betrixaban expected	Administer an initial single dose of betrixaban 80 mg followed by betrixaban 40 mg once daily.
	DRV/c, DRV/r	↔ betrixaban expected	No dose adjustment necessary.
	TPV/r	No data	No dosing recommendations available at this time. Consider alternative ARV or warfarin.
Dabigatran	ATV/c, ATV/r, LPV/r	↑ dabigatran expected With COBI 150 mg Alone: • Dabigatran AUC ↑ 110% to 127%	Dabigatran dosing recommendation depends on indication and renal function. Refer to dabigatran dosing instructions for concomitant use with P-gp inhibitors in dabigatran prescribing information.
	DRV/c, DRV/r	↔ dabigatran expected	No dose adjustment necessary.
	TPV/r	No data	No dosing recommendations available at this time. Consider alternative ARV or warfarin.
Edoxaban	ATV/c, ATV/r, LPV/r	↑ edoxaban expected	Stroke Prevention in Nonvalvular Atrial Fibrillation Indication: • No dose adjustment necessary. Deep Venous Thrombosis and Pulmonary Embolism Indication: • Administer edoxaban 30 mg once daily
	DRV/c, DRV/r	↔ edoxaban expected	No dose adjustment necessary.
	TPV/r	No data	No dosing recommendations available at this time. Consider alternative ARV or warfarin.
Rivaroxaban	PI/c, PI/r	↑ rivaroxaban expected	**Coadministration is not recommended.**
Ticagrelor	All PIs	↑ ticagrelor expected	**Coadministration is not recommended.**
Vorapaxar	All PIs	↑ vorapaxar expected	**Coadministration is not recommended.**

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 3 of 19)

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Anticoagulants and Antiplatelets, continued			
Warfarin	PI/r	↓ warfarin possible	Monitor INR closely when stopping or starting PI/c and adjust warfarin dose accordingly. If switching between RTV and COBI, the effect of COBI on warfarin is not expected to be equivalent to RTV's effect on warfarin.
	PI/c	No data	
Anticonvulsants			
Carbamazepine	ATV (unboosted)	May ↓ PI levels substantially	**Do not coadminister.** Consider alternative anticonvulsant or ARV.
	ATV/r, LPV/r, TPV/r	↑ carbamazepine possible TPV/r ↑ carbamazepine AUC 26% May ↓ PI levels substantially	Consider alternative anticonvulsant or monitor levels of both drugs and assess virologic response. **Do not coadminister with LPV/r once daily.**
	DRV/r	Carbamazepine AUC ↑ 45% DRV: no significant change	Monitor anticonvulsant level and adjust dose accordingly.
	PI/c	↑ carbamazepine possible ↓ cobicistat expected ↓ PI levels expected	**Contraindicated.**
Eslicarbazepine, Oxcarbazepine	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 ethosuximide 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	
	PI/c	No data	Monitor anticonvulsant level and adjust dose accordingly.
Phenobarbital	PI/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.**

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 4 of 19)

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Anticonvulsants, continued			
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.
	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.**
	PI/c	↓ cobicistat expected ↓ PI levels expected	**Contraindicated.**
Valproic Acid (VPA)	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)			
Aripiprazole	PI/c, PI/r	↑ aripiprazole expected	Administer 25% of the usual aripiprazole dose. Titrate dose based on clinical monitoring for efficacy/toxicity. Refer to aripiprazole label for doses to use in patients who have major depressive disorder or who are known to be CYP2D6 poor metabolizers.
	ATV (unboosted)	↑ aripiprazole expected	Administer 50% of the usual aripiprazole dose. Titrate based on clinical monitoring for efficacy/toxicity. Refer to aripiprazole label for doses to use in patients who have major depressive disorder or who are known to be CYP2D6 poor metabolizers.
Brexpiprazole	PI/c, PI/r	↑ brexpiprazole expected	Administer 25% of the usual brexpiprazole dose. Titrate based on clinical monitoring for efficacy/toxicity. Refer to brexpiprazole label for doses to use in patients who have major depressive disorder or who are known to be CYP2D6 poor metabolizers.
	ATV (unboosted)	↑ brexpiprazole expected	Administer 50% of the usual brexpiprazole dose. Titrate based on clinical monitoring for efficacy/toxicity. Refer to brexpiprazole label for doses to use in patients who have major depressive disorder or who are known to be CYP2D6 poor metabolizers.
Bupropion	LPV/r	Bupropion AUC ↓ 57%	Titrate bupropion dose based on clinical response.
	TPV/r	Bupropion AUC ↓ 46%	
	ATV/r, DRV/r	↓ bupropion possible	
	PI/c	↔ bupropion expected	No dose adjustment necessary.
Buspirone	All PIs	↑ buspirone expected	Use a low dose of buspirone with caution and titrate buspirone dose based on clinical response.

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 5 of 19)

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antidepressants, Anxiolytics, and Antipsychotics (also see Sedative/Hypnotics section below), continued			
Cariprazine	All PIs	↑ cariprazine expected	Starting Cariprazine in a Patient Already Receiving a PI: • Administer cariprazine 1.5 mg on Day 1 and Day 3, with no dose given on Day 2. From Day 4 onward, administer cariprazine 1.5 mg daily. Dose can be increased to a maximum dose of cariprazine 3 mg daily. If the PI is withdrawn, cariprazine dose may need to be increased. Starting a PI in a Patient Already Receiving Cariprazine: • For patients receiving cariprazine 3 mg or cariprazine 6 mg daily, reduce dose by half. For patients taking cariprazine 4.5 mg daily, the dose should be reduced to cariprazine 1.5 mg or cariprazine 3 mg daily. For patients taking cariprazine 1.5 mg daily, change to cariprazine 1.5 mg every other day. If PI is withdrawn, cariprazine dose may need to be increased.
Fluvoxamine	All PIs	↑ fluvoxamine possible	Titrate fluvoxamine dose based on clinical response.
Lurasidone	PI/c, PI/r	↑ lurasidone expected	**Contraindicated.**
	ATV (unboosted)	↑ lurasidone expected	Consider alternative therapy. If coadministration is necessary, reduce lurasidone dose by 50%.
Pimavanserin	All PIs	↑ pimavanserin expected	Reduce dose from pimavanserin 34 mg daily to pimavanserin 17 mg daily.
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.
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 (TCA) Amitriptyline, desipramine, doxepin, imipramine, nortriptyline	All PIs	↑ TCA expected	Use lowest possible TCA dose and titrate based on clinical assessment and/or drug levels.
Other Antipsychotics (CYP3A4 and/or CYP2D6 substrates)	PI/c, PI/r	↑ antipsychotic possible	Titrate antipsychotic dose using the lowest initial dose, or adjust maintenance dose accordingly. Monitor for toxicities.
Other Selective Serotonin Reuptake Inhibitors (SSRIs) (e.g., citalopram, escitalopram, fluoxetine, paroxetine, sertraline)	DRV/r	Paroxetine AUC ↓ 39% Sertraline AUC ↓ 49%	Titrate SSRI dose based on clinical response.
	ATV/r, LPV/r, TPV/r	No data	
	PI/c	Effects unknown	Titrate SSRI dose using the lowest available initial or maintenance dose.

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
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 dose adjustments. Doses >200 mg/day **are not recommended** with PI/r, ATV/c, or DRV/c unless dosing is guided by itraconazole levels.
Posaconazole	ATV/r	ATV AUC ↑ 146% ↑ posaconazole possible	If coadministered, monitor for PI adverse effects. Consider monitoring for posaconazole concentrations and toxicities.
	ATV	ATV AUC ↑ 268% ↑ posaconazole possible	
	ATV/c, DRV/c, DRV/r, LPV/r, TPV/r	↑ PI possible ↑ posaconazole possible	
Voriconazole	ATV (unboosted)	↑ voriconazole possible ↑ PI possible	Monitor for toxicities.
	All PI/r	RTV 100 mg BID ↓ voriconazole AUC 39%	Do not coadminister voriconazole and RTV or COBI unless benefit outweighs risk. If coadministered, consider monitoring voriconazole concentration and adjust dose accordingly.
	PI/c	Effect on voriconazole unknown	
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 dose to canagliflozin 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%	

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 7 of 19)

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antimalarials, continued			
Artesunate/ Mefloquine	LPV/r	Dihydroartemisinin AUC ↓ 49% Mefloquine AUC ↓ 28% ↔ LPV	Clinical significance unknown. If used, monitor closely for antimalarial efficacy.
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.

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 8 of 19)

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antimycobacterials (for treatment of *Mycobacterium tuberculosis* and nontuberculosis mycobacterial infections), continued			
Rifabutin	ATV (unboosted)	↑ rifabutin AUC 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 healthy study participants.
	ATV/r	Compared with Rifabutin (300 mg Once Daily) Alone, Rifabutin (150 mg Once Daily) plus ATV/r: • Rifabutin AUC ↑ 110% and metabolite AUC ↑ 2,101%	
	DRV/r	Compared with Rifabutin (300 mg Once Daily) Alone, Rifabutin (150 mg Every Other Day) plus DRV/r: • Rifabutin AUC ↔ and metabolite AUC ↑ 881%	
	LPV/r	Compared with Rifabutin (300 mg daily) Alone, Rifabutin (150 mg Once Daily) plus LPV/r: • Rifabutin AUC ↑ 203% and metabolite AUC ↑ 375%	
	TPV/r	Rifabutin AUC ↑ 190% and metabolite AUC ↑ 1,971%	
	PI/c	↑ rifabutin expected	
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 levels.
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.**

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 9 of 19)

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Cardiac Medications, continued			
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).
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/c , PI/r	RTV (200 mg BID) ↑ digoxin AUC 29% and ↑ half-life 43% DRV/r ↑ digoxin AUC 36% COBI ↑ digoxin C_{max} 41% and ↔ 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.**

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 10 of 19)

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
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 adverse effects associated with corticosteroids.** Consider an alternative corticosteroid (e.g., beclomethasone).
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 adverse effects associated with systemic corticosteroids.**
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 adverse effects associated with systemic corticosteroids. If coadministered, monitor for adrenal insufficiency, Cushing's syndrome, and other corticosteroid-associated toxicities.
	All PIs	↑ prednisolone possible	
Betamethasone, Methylprednisolone, 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 plus Paritaprevir/ Ombitasvir/RTV	ATV (unboosted)	↔ ATV	ATV 300 mg alone, **without COBI or additional RTV**, should be given in the morning with dasabuvir plus 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 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 11 of 19)

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
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 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 12 of 19)

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hepatitis C Direct-Acting Antiviral Agents, continued			
Simeprevir	All PIs	Compared with Simeprevir 150 mg Alone, Simeprevir 50 mg plus DRV/r 800 mg/100 mg Daily: • Simeprevir AUC ↑ 159% RTV 100 mg BID ↑ simeprevir AUC 618%	**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/c , DRV/r	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.**

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 13 of 19)

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
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[b] or recommend alternative contraceptive method. Oral contraceptives containing less than 25 mcg of ethinyl estradiol or progestins other than norethindrone or norgestimate have not been studied.
	ATV/r	Ethinyl estradiol AUC ↓ 19% and C_{min} ↓ 37% Norgestimate ↑ 85% Norethindrone AUC ↑ 51% and C_{min} ↑ 67%	Oral contraceptive should contain at least 35 mcg of ethinyl estradiol.[c] 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 drospirenone-containing hormonal contraceptive 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 MPA Injectable	LPV/r	MPA AUC ↑ 46% No significant change in C_{min}	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.
Etonogestrel/ Ethinyl Estradiol Vaginal Ring	ATV/r	Ethinyl estradiol AUC ↓ 26% Etonogestrel AUC ↑ 79%	Use standard dose.
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.

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hormonal Therapies, continued			
Menopausal Hormone Replacement Therapy (HRT)	All PIs	↓ estrogen possible with estradiol or conjugated estrogen (equine and synthetic)	Adjust estrogen dosage as needed based on clinical effects.
	All PIs	↑ drospirenone possible ↑ medroxyprogesterone ↑ micronized progesterone See Hormonal Contraceptives for other progestin-PI interactions	Adjust progestin/progesterone dosage as needed based on clinical effects. Because drospirenone is prescribed as a lower dose for menopausal HRT than the products used for hormonal contraceptives, it is not contraindicated with ATV/c products.
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 (unboosted), ATV/r	↑ atorvastatin possible	Titrate atorvastatin dose carefully and use lowest dose necessary while monitoring for toxicities.
	ATV/c	Atorvastatin AUC ↑ 9.2-fold, C_{max} ↑ 18.9-fold	**Coadministration is not recommended.**
	DRV/r	DRV/r plus atorvastatin 10 mg similar to atorvastatin 40 mg administered alone	Titrate atorvastatin dose carefully and use the lowest dose necessary while monitoring for toxicities. Do not exceed 20 mg atorvastatin daily.
	DRV/c	Atorvastatin AUC ↑ 3.9-fold, C_{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% and C_{max} ↑ 60% ↔ ATV DRV/r ↓ pitavastatin AUC 26% ↔ DRV/r LPV/r ↓ pitavastatin AUC 20% ↔ LPV	No dose adjustment necessary.

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 15 of 19)

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
HMG-CoA Reductase Inhibitors, continued			
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 • Pravastatin AUC ↑ 23% at steady state	Titrate pravastatin dose carefully while monitoring for toxicities.
	LPV/r	Pravastatin AUC ↑ 33%	No dose adjustment necessary.
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 rosuvastatin 10 mg 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 dose necessary while monitoring for toxicities. Do not exceed rosuvastatin 20 mg 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 rosuvastatin 10 mg 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.

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 16 of 19)

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
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.**
	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.
	DRV/r	No significant effect on buprenorphine Norbuprenorphine[d] AUC ↑ 46% and C_{min} ↑ 71%	No dose adjustment necessary. Clinical monitoring is recommended. When transferring buprenorphine from transmucosal delivery to implantation, monitor to ensure buprenorphine effect is adequate and not excessive.
	LPV/r	No significant effect	
	TPV/r	No significant effect on buprenorphine Norbuprenorphine[d] AUC, C_{max}, and C_{min} ↓ 80% TPV C_{min} ↓ 19% to 40%	Consider monitoring TPV level. When transferring buprenorphine from transmucosal delivery to implantation, monitor to ensure buprenorphine effect is adequate and not excessive.
	PI/c	Effects unknown	Titrate buprenorphine dose using the lowest initial dose. Dose adjustment of buprenorphine may be needed. It may be necessary to remove implant and treat with a formulation that permits dose adjustments. Clinical monitoring is recommended.
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.
	PI/c	Effects unknown	Titrate methadone dose using the lowest feasible initial dose. Dose adjustment of methadone may be needed. Clinical monitoring is recommended.
	All PI/r	ATV/r and DRV/r ↓ R-methadone[e] AUC 16% to 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	All PIs	↑ tramadol possible	Tramadol dose reduction may be necessary. Monitor for tramadol toxicities and clinical response.

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 17 of 19)

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
PDE5 Inhibitors			
Avanafil	All PIs except unboosted ATV	RTV (600 mg BID for 5 days) ↑ avanafil AUC 13-fold and ↑ 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 plus sildenafil 25 mg similar to sildenafil 100 mg alone RTV 500 mg BID ↑ sildenafil AUC 1,000%	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% No significant effect on TPV/r steady state	For Treatment of Erectile Dysfunction: • Start with tadalafil 5-mg dose and do not exceed a single dose of tadalafil 10 mg every 72 hours. Monitor for adverse effects of tadalafil. For Treatment of PAH *In Patients on a PI >7 Days:* • Start with tadalafil 20 mg once daily and increase to tadalafil 40 mg once daily based on tolerability. *In Patients on Tadalafil who Require a PI:* • Stop tadalafil ≥24 hours before PI initiation. Seven days after PI initiation, restart tadalafil at 20 mg once daily and increase to tadalafil 40 mg once daily based on tolerability. *In Patients Switching between COBI and RTV:* • Maintain tadalafil dose. For Treatment of Benign Prostatic Hyperplasia: • Maximum recommended daily dose is tadalafil 2.5 mg per day.
Vardenafil	All PIs	RTV 600 mg BID ↑ vardenafil AUC 49-fold	Start with vardenafil 2.5 mg every 72 hours and monitor for adverse effects of vardenafil.
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	**Oral midazolam is contraindicated with 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.**

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 18 of 19)

Concomitant Drug	PI	Effect on PI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Sedative/Hypnotics, continued			
Triazolam	All PIs	↑ triazolam expected RTV (200 mg BID) ↑ triazolam half-life 1,200% and AUC 2,000%	**Contraindicated.**
Zolpidem	PI/c, PI/r	↑ zolpidem possible	Initiate zolpidem at a low dose. Dose reduction may be necessary.
Miscellaneous Drugs			
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% and C_{max} 184% Significant ↑ colchicine expected with all PIs, with or without COBI or RTV	For Treatment of Gout Flares: • Administer a single dose of colchicine 0.6 mg, followed by colchicine 0.3 mg 1 hour later. Do not repeat dose for at least 3 days. For Prophylaxis of Gout Flares: • Administer 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 colchicine 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.
Enzalutamide	All PIs	↓ PI expected	**Contraindicated.**
Ergot Derivatives	All PIs	↑ dihydroergotamine, ergotamine, methylergonovine expected	**Contraindicated.**
Flibanserin	All PIs	↑ flibanserin expected	**Contraindicated.**
Irinotecan	ATV (unboosted), ATV/c, ATV/r	↑ irinotecan expected	**Contraindicated.**
Mitotane	All PIs	↓ PI expected	**Contraindicated.**
Salmeterol	All PIs	↑ salmeterol possible	**Do not coadminister** because of potential increased risk of salmeterol-associated CV events.

Table 21a. Drug Interactions Between Protease Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 19 of 19)

[a] DHA is an active metabolite of artemether.

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

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

[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 = cobicistat; CrCl = creatinine clearance; CV = cardiovascular; CYP = cytochrome P; DHA = dihydroartemisinin; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; ECG = electrocardiogram; eGFR = estimated glomerular filtration rate; FPV = fosamprenavir; HCV = hepatitis C virus; HRT = hormone replacement therapy; IDV = indinavir; INR = international normalized ratio; LPV = lopinavir; LPV/r = lopinavir/ritonavir; MPA = medroxyprogesterone acetate; NFV = nelfinavir; OATP = organic anion-transporting polypeptide; PAH = pulmonary arterial hypertension; PDE5 = Phosphodiesterase Type 5; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; PK = pharmacokinetic; PPI = proton pump inhibitor; PTH = parathyroid hormone; QTc = QT corrected for heart rate; RTV = ritonavir; SQV = saquinavir; TDF = tenofovir disoproxil fumarate; TPV = tipranavir; TPV/r = tipranavir/ritonavir

Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 1 of 10)

This table provides information relating to PK interactions between NNRTIs and non-ARV drugs. For interactions between ARV agents and for dosing recommendations, refer to Tables 21c, 22a, and 22b. Recommendations for managing a particular drug interaction may differ depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or if a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly.

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

Concomitant Drug Class/ Name	NNRTI[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% and C_{min} ↓ 33%	**Contraindicated. Do not coadminister.**
Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia			
Alfuzosin, Doxazosin, Silodosin	EFV, ETR, NVP	↓ alpha antagonist expected	Consider alternative therapy. If coadministration is necessary, monitor for therapeutic effectiveness of alpha antagonist.
Tamsulosin	EFV, ETR, NVP	↓ tamsulosin expected	Monitor for therapeutic effectiveness of tamsulosin after 2 to 4 weeks of dosing. May need to increase to tamsulosin 0.8 mg once daily for patients who fail to respond to the 0.4 mg dose.
Anticoagulants/Antiplatelets			
Apixaban	EFV, ETR, NVP	↓ apixaban possible	Consider alternative therapy.
Betrixaban	All NNRTIs	↔ betrixaban expected	No dose adjustment necessary.
Clopidogrel	EFV, ETR	↓ activation of clopidogrel possible	ETR may prevent metabolism of clopidogrel (inactive) to its active metabolite. Avoid coadministration, if possible.
	DOR, NVP, RPV	↔ clopidogrel expected	No dose adjustment necessary.
Dabigatran	All NNRTIs	↔ dabigatran expected	No dose adjustment necessary.
Edoxaban	All NNRTIs	↔ edoxaban expected	No dose adjustment necessary.
Prasugrel	All NNRTIs	↔ 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 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 2 of 10)

Concomitant Drug Class/ Name	NNRTI[a]	Effect on NNRTI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Anticonvulsants			
Carbamazepine, Phenobarbital, Phenytoin	EFV	Carbamazepine plus EFV: • Carbamazepine AUC ↓ 27% • EFV AUC ↓ 36% Phenytoin plus EFV: • ↓ EFV • ↓ phenytoin possible	Monitor anticonvulsant and EFV concentrations 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 concentrations and virologic responses or consider alternative anticonvulsant.
	DOR, RPV	↓ NNRTI possible	**Contraindicated. Do not coadminister.** Consider alternative anticonvulsant.
Eslicarbazepine	All NNRTIs	↓ NNRTI possible	Monitor virologic outcomes and consider monitoring plasma concentrations of ARVs, or consider alternative anticonvulsant or ARV drug.
Oxcarbazepine	DOR, RPV	↓ NNRTI 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	All NNRTIs	↔ antidepressant expected	No dose adjustment necessary.
Paroxetine	EFV, ETR	↔ paroxetine observed with EFV or ETR	No dose adjustment necessary.
	DOR, NVP, RPV	↔ expected with DOR, NVP or RPV	No dose adjustment necessary.
Nefazodone	EFV, ETR, NVP	↓ nefazodone expected ↑ NNRTI possible	Monitor the antidepressant effect and titrate dose as necessary. Monitor for ARV-related adverse events.
	DOR, RPV	↑ NNRTI possible	Monitor for ARV-related adverse events.
Sertraline	EFV	Sertraline AUC ↓ 39%	Titrate sertraline dose based on clinical response.
Trazodone	EFV, ETR, NVP	↓ trazodone possible	Monitor the therapeutic effect of trazodone and titrate dose as necessary.

Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 3 of 10)

Concomitant Drug Class/ Name	NNRTI[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.
	DOR,RPV	↑ NNRTI possible	No dose adjustment necessary.
Isavuconazole	EFV, ETR, NVP	↓ isavuconazole possible	Dose adjustments for isavuconazole may be necessary. Consider monitoring isavuconazole concentration and antifungal response.
	DOR, RPV	↑ NNRTI possible	No dose adjustment necessary.
Itraconazole	EFV	Itraconazole and OH-itraconazole AUC, C_{max}, and C_{min} ↓ 35% to 44%	Failure to achieve therapeutic itraconazole concentrations has been reported. Avoid this combination if possible. If coadministered, closely monitor itraconazole concentration and adjust dose accordingly.
	ETR	↓ itraconazole possible ↑ ETR possible	Dose adjustments for itraconazole may be necessary. Monitor itraconazole level and antifungal response.
	NVP	Itraconazole AUC ↓ 61% ↑ NVP possible	Avoid this combination if possible. If coadministered, monitor itraconazole concentration and adjust dose accordingly.
	DOR, RPV	↑ NNRTI 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.
	DOR, 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 ETR AUC ↑ 36%	No dose adjustment necessary.
	NVP	↓ voriconazole possible ↑ NVP possible	Monitor for toxicity and antifungal response and/or voriconazole concentration.
	DOR, RPV	↑ NNRTI possible	No dose adjustment necessary.
Antihyperglycemics			
Canagliflozin, Dapagliflozin, Empagliflozin, Sitagliptin	All NNRTIs	↔ antihyperglycemic expected	No dose adjustment necessary.
Linagliptin, Saxagliptin	EFV, ETR, NVP	↓ antihyperglycemic possible	Monitor glycemic control.

Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 4 of 10)

Concomitant Drug Class/ Name	NNRTI[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.
	ETR	Artemether AUC ↓ 38% ↔ DHA AUC ↔ Lumefantrine AUC ↔ ETR AUC	Clinical significance of the reduced antimalarial drug concentrations unknown. If used in combination with ETR, monitor for antimalarial efficacy.
	NVP	Artemether AUC ↓ 67% to 72% DHA: • Study results are conflicting. DHA AUC ↓ 37% in one study, no difference in another. Lumefantrine: • Study results are conflicting. Lumefantrine AUC ↓ 25% to 58% in 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	DOR	DOR AUC ↓ 50%	Increase DOR dose to 100 mg twice daily. No dose adjustment for 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 ETR AUC ↓ 37%	**Do not coadminister ETR plus PI/r with rifabutin.** Use rifabutin 300 mg once daily if ETR is administered without PI/r

Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 5 of 10)

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

Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 6 of 10)

Concomitant Drug Class/ Name	NNRTI[a]	Effect on NNRTI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
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 AUC	No dose adjustment necessary.
	ETR, NVP	↔ lorazepam expected	
Midazolam	EFV	↑ or ↓ midazolam possible	Monitor therapeutic effectiveness and toxicity of midazolam.
	ETR	Midazolam AUC ↓ 31% Midazolam active metabolite C_{max} ↑ 57%	Monitor therapeutic effectiveness of midazolam.
	NVP	↓ midazolam possible	Monitor therapeutic effectiveness of midazolam.
Triazolam	EFV, ETR, NVP	↓ triazolam possible	Monitor therapeutic effectiveness of triazolam.
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.
	ETR, NVP	↓ diltiazem or verapamil possible	
Corticosteroids			
Dexamethasone	DOR, EFV, ETR, NVP	↓ NNRTI possible	Consider alternative corticosteroid for long-term use. If dexamethasone is used with NNRTI, monitor virologic response.
	RPV	Significant ↓ RPV possible	**Contraindicated with more than a single dose of dexamethasone.**
Hepatitis C Direct-Acting Antiviral Agents			
Daclatasvir	EFV, ETR, NVP	Daclatasvir 120 mg Once Daily plus EFV 600 mg Daily Compared with Daclatasvir 60 mg Alone: • Daclatasvir C_{min} ↓ 17%, AUC ↑ 37%	The recommended dose is daclatasvir 90 mg once daily.
	DOR, RPV	No data	No dose adjustment necessary.
Dasabuvir plus Paritaprevir/ Ombitasivir/RTV	DOR	↑ DOR possible	No dose adjustment necessary.
	EFV	No data	**Contraindicated.**
	ETR, NVP	↓ DAAs possible	**Do not coadminister.**
	RPV	RPV AUC ↑ 150% to 225%	**Do not coadminister,** due to potential for QT interval prolongation with higher concentrations of RPV.

Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 7 of 10)

Concomitant Drug Class/ Name	NNRTI[a]	Effect on NNRTI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hepatitis C Direct-Acting Antiviral Agents, continued			
Elbasvir/ Grazoprevir	EFV	Elbasvir AUC ↓ 54% Grazoprevir AUC ↓ 83% EFV ↔ by grazoprevir EFV ↔ AUC by elbasvir	**Contraindicated.**
	ETR, NVP	↓ elbasvir and grazoprevir expected	**Do not coadminister.**
	DOR, RPV	↔ Elbasvir, grazoprevir ↔ DOR, RPV	No dose adjustment necessary.
Glecaprevir/ Pibrentasvir	DOR	↑ DOR expected	No dose adjustment necessary.
	EFV	↓ glecaprevir and pibrentasvir expected	**Do not coadminister.**
	ETR , NVP	↓ glecaprevir and pibrentasvir possible	
	RPV	↔ glecaprevir, pibrentasvir RPV AUC ↑ 84%	No dose adjustment necessary.
Ledipasvir/ Sofosbuvir	EFV	Ledipasvir AUC, C_{min}, and C_{max} ↓ 34% ↔ sofosbuvir	No dose adjustment necessary.
	ETR, NVP	No significant effect expected	
	DOR, RPV	↔ Ledipasvir, sofosbuvir ↔ DOR, RPV	
Simeprevir	DOR	No significant effect expected.	No dose adjustment necessary.
	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.**
	DOR, 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.**
	DOR, RPV	No signficant effect expected	No dose adjustment necessary.

Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 8 of 10)

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

Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 9 of 10)

Concomitant Drug Class/ Name	NNRTI[a]	Effect on NNRTI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hormonal Therapies, continued			
Menopausal Hormone Replacement Therapy	EFV, ETR, NVP	↓ estrogen possible with estradiol or conjugated estrogen (equine and synthetic) ↓ medroxyprogesterone possible ↓ micronized progesterone possible ↓ drospirenone possible See Hormonal Contraceptives for other progestin-NNRTI interactions	Monitor menopausal symptoms. Titrate to the dose of hormonal therapy that achieves 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 titrate dosing as necessary to achieve therapeutic goals.
	EFV, ETR, NVP	↓ testosterone possible	Monitor masculinizing effects of testosterone and titrate testosterone dose as necessary to achieve therapeutic goals.
HMG-CoA Reductase Inhibitors			
Atorvastatin	EFV, ETR	Atorvastatin AUC ↓ 32% to 43%	Adjust atorvastatin dose according to lipid response, but do not exceed the maximum recommended dose.
	NVP	↓ atorvastatin possible	Adjust atorvastatin dose according to lipid response, but do not exceed the maximum recommended dose.
	DOR, RPV	↔ atorvastatin AUC	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 response, but do not exceed the maximum recommended dose. If EFV is used with a PI/r, simvastatin and lovastatin should be avoided.
	ETR, NVP	↓ 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.
Pitavastatin	EFV	↔ pitavastatin AUC	No dose adjustment necessary.
	DOR, ETR, NVP, RPV	↔ pitavastatin expected	No dose adjustment necessary.
Pravastatin	EFV	Pravastatin 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.

Table 21b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 10 of 10)

Concomitant Drug Class/ Name	NNRTI[a]	Effect on NNRTI and/ or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
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.
	DOR, ETR	No significant effect	No dose adjustment necessary.
	NVP	Methadone AUC ↓ 37% to 51% No significant effect on NVP	Opioid withdrawal is common; increased methadone dose is often necessary.
	RPV	R-methadone[c] AUC ↓ 16%	No dose adjustment necessary, but monitor for withdrawal symptoms.
PDE5 Inhibitors			
Sildenafil	DOR, RPV	↔ sildenafil expected	No dose adjustment necessary.
	ETR	Sildenafil AUC ↓ 57%	May need to titrate sildenafil dose based on clinical effect.
	EFV, NVP	↓ sildenafil possible	
Tadalafil	EFV, ETR, NVP	↓ tadalafil possible	May need to titrate tadalafil dose based on clinical effect.
	RPV	↔ tadalafil	No dose adjustment necessary.
Avanafil, Vardenafil	EFV, ETR, NVP	↓ PDE5 inhibitor possible	May need to increase PDE5 inhibitor dose based on clinical effect.
Miscellaneous Drugs			
Enzalutamide	All NNRTIs	↓ NNRTI expected	**Contraindicated.**
Mitotane	All NNRTIs	↓ NNRTI expected	**Contraindicated.**

[a] Approved dose for RPV is 25 mg once daily. Most PK interaction studies were performed using 75 mg 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 blocker; C_{max} = maximum plasma concentration; C_{min} = minimum plasma concentration; DAA = direct-acting antiviral; DHA = dihydroartemisinin; DMPA = depot medroxyprogesterone acetate; DOR = doravirine; EFV = efavirenz; ETR = etravirine; HMG-CoA = hydroxy-methylglutaryl-coenzyme A; INR = international normalized ratio; MAC = *Mycobacterium avium* complex; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; OH-itraconazole = active metabolite of itraconazole; PCP = *Pneumocystis jirovecii* pneumonia; PDE5 = phosphodiesterase type 5; PI = protease inhibitor; PI/r = protease inhibitor/ritonavir; PK = pharmacokinetic; PPI = proton pump inhibitor; RPV = rilpivirine; RTV = ritonavir

Table 21c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents) (Last updated October 25, 2018; last reviewed October 25, 2018)
(page 1 of 3)

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

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

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

Table 21c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents) (Last updated October 25, 2018; last reviewed October 25, 2018)
(page 2 of 3)

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 necessary.
	ZDV	ZDV AUC ↑ 29% to 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	**Coadministration is not recommended.**
Antimycobacterial Rrifampin	TAF	TAF AUC ↓ 55% TFV-DP (intracellular active moiety) AUC ↓ 36% TAF plus Rifampin Compared with TDF Alone: • TFV-DP (intracellular active moiety) AUC ↑ 4.2-fold With Twice-Daily TAF 25 mg Compared with Once-Daily TAF without Rifampin: • TAF AUC ↓ 14% • TFV-DP (intracellular active moiety) AUC ↓ 24%	**Coadministration is not recommended.**
	TDF	↔ AUC TFV	No dose adjustment necessary.
Rifabutin, Rifapentine	TAF	↓ TAF possible	**Coadministration is not recommended.**
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) TFV AUC ↑ 24% to 37%	**Avoid concomitant use without RTV or COBI.** Dose: • ATV 300 mg daily plus (RTV 100 mg or COBI 150 mg) daily when coadministered with TDF 300 mg daily • If using TDF and H2 receptor antagonist in an ART-experienced patient, use ATV 400 mg daily plus (RTV 100 mg or COBI 150 mg) daily Monitor for TDF-associated toxicity.
	ZDV	With ATV (Unboosted): • ZDV C_{min} ↓ 30% and ↔ ZDV AUC	Clinical significance unknown.

Table 21c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents) (Last updated October 25, 2018; last reviewed October 25, 2018)
(page 3 of 3)

Concomitant Drug Class/ Name	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosage Recommendations and Clinical Comments
PIs (HIV), continued			
DRV/c	TAF	TAF 25 mg with DRV/c: • ↔ TAF	No dose adjustment necessary.
	TDF	↑ TDF possible	Monitor for TDF-associated toxicity.
DRV/r	TAF	TAF 10 mg with DRV/r: • ↔ TAF	No dose adjustment necessary.
	TDF	TFV AUC ↑ 22% and C_{min} ↑ 37%	Clinical significance unknown. Monitor for TDF-associated toxicity.
LPV/r	TAF	TAF 10 mg with DRV/r: • TAF AUC ↑ 47%	No dose adjustment necessary.
	TDF	↔ LPV/r AUC TFV AUC ↑ 32%	Clinical significance unknown. Monitor for TDF-associated toxicity.
TPV/r	ABC	ABC AUC ↓ 35% to 44%	Appropriate doses for this combination have not been established.
	TAF	↓ TAF expected	**Coadministration is not recommended.**
	TDF	↔ TDF AUC TPV AUC ↓ 9% to 18% and C_{min} ↓ 12% to 21%	No dose adjustment necessary.
	ZDV	ZDV AUC ↓ 31% to 42% ↔ TPV AUC	Appropriate doses for this combination have not been established.

Key to Symbols:

↑ = increase

↓ = decrease

↔ = no change

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; C_{min} = minimum plasma concentration; COBI = cobicistat; d4T = stavudine; ddI = didanosine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; FDA = Food and Drug Administration; FTC = emtricitabine; HCV = hepatitis C virus; INSTI = integrase strand transfer inhibitors; LPV/r = lopinavir/ritonavir; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TFV = tenofovir; TFV-DP = tenofovir diphosphate; TPV/r = tipranavir/ritonavir; ZDV = zidovudine

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 1 of 15)

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

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

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 2 of 15)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers, continued			
Al, Mg, +/- Ca-Containing Antacids, continued Please refer to the Miscellaneous Drugs section of this table for recommendations on use with other polyvalent cation products (e.g., Fe, Ca supplements, multivitamins).	RAL	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	BIC, DTG, EVG/c	No significant effect	No dose adjustment necessary.
	RAL	RAL AUC ↑ 44% and C_{max} ↑ 60%	No dose adjustment necessary.
PPIs	BIC, DTG, EVG/c	No significant effect	No dose adjustment necessary.
	RAL	RAL AUC ↑ 37% and C_{min} ↑ 24%	No dose adjustment necessary.
Anticoagulants and Antiplatelets			
Apixaban	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ apixaban expected	In Patients Requiring Apixaban 2.5 mg Twice Daily: • **Coadministration is not recommended.** In Patients Requiring Apixaban 5 mg or 10 mg Twice Daily: • Reduce apixaban dose by 50%.
Betrixaban	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ betrixaban expected	Administer initial single dose of betrixaban 80 mg, followed by betrixaban 40 mg once daily.
Dabigatran	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ dabigatran expected Dabigatran AUC ↑ 110% to 127% with COBI 150 mg alone	Dabigatran dosing recommendation depends on indication and renal function. Refer to dabigatran prescribing information for dosing instruction when used with P-gp inhibitors.
Edoxaban	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↔ or ↑ edoxaban expected	For Stroke Prevention in Nonvalvular Atrial Fibrillation: • No dose adjustment necessary. For Deep Venous Thrombosis and Pulmonary Embolism: • Administer edoxaban 30 mg once daily.
Rivaroxaban	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ rivaroxaban expected	**Coadministration is not recommended.**

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 3 of 15)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Anticoagulants and Antiplatelets, continued			
Ticagrelor	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ ticagrelor expected	**Coadministration is not recommended.**
Vorapaxar	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ vorapaxar expected	**Coadministration is not recommended.**
Warfarin	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ or ↓ warfarin possible	Monitor INR and adjust warfarin dose accordingly.
Anticonvulsants			
Carbamazepine	BIC	↓ BIC possible	Consider using an alternative anticonvulsant or ARV.
	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.**
Eslicarbazepine	All INSTIs	↓ INSTI possible ↓ COBI possible	Consider using an alternative anticonvulsant or ARV.
Ethosuximide	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ ethosuximide possible	Clinically monitor for ethosuximide toxicities.
Lamotrigine	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	No data	Monitor anticonvulsant level and adjust dose accordingly.
Oxcarbazepine	All INSTIs	↓ INSTI possible ↓ COBI possible	Consider using an alternative anticonvulsant or ARV.
Phenobarbital **Phenytoin**	BIC	↓ BIC possible	**Coadministration is not recommended.**
	DTG	↓ DTG possible	**Coadministration is not recommended.**
	EVG/c	↓ EVG/c expected	**Contraindicated.**
	RAL	↓ or ↔ RAL possible	**Coadministration is not recommended.**
Valproic Acid	All INSTIs	No data	Monitor valproic acid concentration and virologic response.

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 4 of 15)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antidepressants/Anxiolytics/Antipsychotics Also see Sedative/Hypnotics section below.			
Aripiprazole	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ aripiprazole expected	Administer 25% of the usual aripiprazole dose. Titrate based on clinical monitoring for efficacy and toxicity. Refer to aripiprazole label for dosing recommendations in patients who are known to be CYP2D6 poor metabolizers or who have major depressive disorder.
Brexpiprazole	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ brexpiprazole expected	Administer 25% of the usual brexpiprazole dose. Titrate based on clinical monitoring for efficacy/toxicity. Refer to brexpiprazole label for dosing recommendations in patients who are known to be CYP2D6 poor metabolizers or who have major depressive disorder.
Bupropion	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ bupropion possible	Titrate bupropion dose based on clinical response.
Buspirone	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ buspirone possible	Initiate buspirone at a low dose. Dose reduction may be necessary.
Cariprazine	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ cariprazine expected	Starting Cariprazine in a Patient Already on EVG/c: • Administer cariprazine 1.5 mg on Day 1 and Day 3, with no dose given on Day 2. • From Day 4 onward, administer 1.5 mg daily. Can be increased to a maximum dose of 3 mg daily. • If EVG/c is withdrawn, cariprazine dose may need to be increased. Starting EVG/c in a Patient Already on Cariprazine: • For patients receiving cariprazine 3 mg or 6 mg daily, reduce cariprazine dose by half. • For patients taking cariprazine 4.5 mg daily, the dose should be reduced to 1.5 mg or 3 mg daily. • For patients taking cariprazine 1.5 mg daily, change to 1.5 mg every other day. • If EVG/c is withdrawn, cariprazine dose may need to be increased.

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 5 of 15)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antidepressants/Anxiolytics/Antipsychotics, continued Also see Sedative/Hypnotics section below.			
Fluvoxamine	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ or ↓ EVG possible	Consider alternative antidepressant or ARV.
Lurasidone	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ lurasidone expected	**Contraindicated.**
Pimavanserin	BIC, DTG, RAL	↔ expected	Standard doses.
	EVG/c	↑ pimavanserin expected	Reduce pimavanserin dose by 50%. Titrate dose based on efficacy and toxicity.
Pimozide	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ pimozide expected	**Contraindicated.**
Quetiapine	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ quetiapine AUC expected	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.
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.
	BIC, DTG, RAL	↔ BIC, DTG, RAL expected ↔ SSRI expected	No dose adjustment necessary.
TCAs Amitriptyline, desipramine, doxepin, imipramine, nortriptyline	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	Desipramine AUC ↑ 65%	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	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ trazodone possible	Initiate with lowest dose of trazodone and titrate dose carefully.
Other Antipsychotics (CYP3A4 and/or CYP2D6 substrates)	EVG/c	↑ antipsychotic possible	Initiate antipsychotic at a low dose. Decrease in antipsychotic dose may be necessary.

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 6 of 15)

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

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 7 of 15)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antimycobacterials, continued			
Rifabutin	BIC	Rifabutin (300 mg Once Daily): • BIC AUC ↓ 38% and C_{min} ↓ 56%	**Do not coadminister.**
	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% and C_{min} ↓ 67%	**Do not coadminister.**
	RAL	RAL AUC ↑ 19% and C_{min} ↓ 20%	No dose adjustment necessary.
Rifampin	BIC	BIC AUC ↓ 75%	**Contraindicated.**
	DTG	Rifampin with DTG 50 mg BID Compared to DTG 50 mg BID Alone: • DTG AUC ↓ 54% and C_{min} ↓ 72% Rifampin with DTG 50 mg BID Compared to DTG 50 mg Once Daily Alone: • DTG AUC ↑ 33% and 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% and C_{min} ↓ 61% Rifampin with RAL 800 mg BID Compared to RAL 400 mg BID Alone: • RAL AUC ↑ 27% and 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	BIC, DTG, EVG/c	Significant ↓ BIC, DTG, EVG, and COBI expected	**Do not coadminister.**
	RAL	Rifapentine 900 mg Once Weekly: • RAL AUC ↑ 71% and C_{min} ↓ 12% Rifapentine 600 mg Once Daily: • RAL C_{min} ↓ 41%	For once-weekly rifapentine, use standard RAL 400 mg BID doses. **Do not coadminister with once-daily rifapentine.**

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 8 of 15)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Cardiac Medications			
Antiarrhythmics Amiodarone, bepridil, digoxin, disopyramide, dronedarone, flecainide, systemic lidocaine, mexilitine, propafenone, quinidine	BIC, DTG	↔ expected for the listed antiarrhythmics, except for disopyramide ↑ disopyramide possible	No dose adjustment necessary. Coadminister with caution. Clinical monitoring is recommended.
	RAL	↔ expected for the listed antiarrhythmics	No dose adjustment necessary.
	EVG/c	↑ antiarrhythmics possible Digoxin C_{max} ↑ 41% and no significant change in AUC	Use antiarrhythmics with caution. TDM, if available, is recommended for antiarrhythmics.
Bosentan	BIC, DTG	↓ BIC, DTG possible	Standard doses.
	RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ bosentan possible	In Patients on EVG/c ≥10 Days: • Start bosentan at 62.5 mg once daily or every other day based on individual tolerability. In Patients on Bosentan Who Require EVG/c: • Stop bosentan ≥36 hours before EVG/c initiation. At least 10 days after initiation of EVG/c, resume bosentan at 62.5 mg once daily or every other day based on individual tolerability.
Beta-blockers (e.g., metoprolol, timolol)	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ beta-blockers possible	Beta-blocker dose may need to be decreased; adjust dose based on clinical response. Consider using beta-blockers that are not metabolized by CYP450 enzymes (e.g., atenolol, labetalol, nadolol, sotalol).
CCBs	BIC	↑ BIC possible with diltiazem ↔ expected for all other CCBs	No dose adjustment necessary.
	DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ CCBs possible	Coadminister with caution. Titrate CCB dose and monitor for CCB efficacy and toxicities. Refer to Table 21a for diltiazem plus ATV/r recommendations.
Dofetilide	BIC, DTG	↑ dofetilide expected	**Contraindicated.**
	RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ dofetilide possible	**Do not coadminister.**
Eplerenone	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ eplerenone expected	**Contraindicated.**
Ranolazine	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ ranolazine expected	**Contraindicated.**
Ivabradine	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ ivabradine expected	**Contraindicated.**

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 9 of 15)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Corticosteroids			
Beclomethasone Inhaled or intranasal	BIC, DTG, EVG/c, RAL	↔ expected	No dose adjustment necessary.
Budesonide, Ciclesonide, Fluticasone, Mometasone Inhaled or intranasal	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	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	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ glucocorticoids possible ↓ EVG 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	BIC	↓ BIC possible	Consider an alternative corticosteroid for long-term use or an alternative ARV. If coadministration is necessary, monitor virologic response to ART.
	DTG, RAL	↔ expected	No dose adjustment necessary.
	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	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	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.
Betamethasone, Methylprednisolone, Prednisolone, Triamcinolone Local injections, including intra-articular, epidural, or intra-orbital	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	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.
	BIC, RAL	No data	No dose adjustment necessary.
Dasabuvir plus Ombitasvir/ Paritaprevir/RTV	BIC, DTG	No data	No dose adjustment necessary.
	EVG/c	No data	**Do not coadminister.**
	RAL	RAL AUC ↑ 134%	No dose adjustment necessary.

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 10 of 15)

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

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 11 of 15)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hormonal Therapies			
Hormonal Contraceptives Oral	BIC, 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 using an alternative contraceptive method.
		↑ drospirenone possible	Clinical monitoring is recommended, due to the potential for hyperkalemia.
Hormonal Contraceptives Non-oral	All INSTIs	No data	No drug-drug interaction studies have been conducted with INSTIs and non-oral routes of hormone administration. It is unclear if oral drug-drug interaction data can be extrapolated beyond oral routes of administration.
Menopausal Hormone Replacement Therapy	BIC, DTG, RAL	With Estradiol or Conjugated Estrogen (Equine and Synthetic): • ↔ estrogen expected ↔ drospirenone, medroxyprogesterone, or micronized progesterone expected	No dose adjustment necessary.
	EVG/c	↓ estrogen expected ↑ drospirenone possible ↑ oral medroxyprogesterone possible ↑ oral micronized progesterone possible	Adjust estrogen and progestin dose as needed based on clinical effects.
Gender-Affirming Hormone Therapy	BIC, DTG, RAL	↔ estrogen expected	No dose adjustment necessary.
	BIC, DTG, EVG/c, RAL	↔ finasteride, goserelin, leuprolide acetate, spironolactone expected	
	EVG/c	↓ estradiol expected ↑ dutasteride possible	Adjust dutasteride dosage as needed based on clinical effects and endogenous hormone concentrations.
	EVG/c	↑ testosterone possible	Monitor masculinizing effects of testosterone and for adverse effects and adjust testosterone dose as necessary.
	BIC, DTG, RAL	↔ testosterone expected	No dose adjustment necessary.
HMG-CoA Reductase Inhibitors			
Atorvastatin	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	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	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	Significant ↑ lovastatin expected	**Contraindicated**.
Pitavastatin, Pravastatin	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	No data	No dose recommendation.

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 12 of 15)

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

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 13 of 15)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
PDE5 Inhibitors, continued			
Tadalafil	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ tadalafil expected	For Treatment of Erectile Dysfunction: • Start with tadalafil 5-mg dose and do not exceed a single dose of tadalafil 10 mg every 72 hours. Monitor for adverse effects of tadalafil. For Treatment of PAH *In Patients on EVG/c >7 Days:* • Start with tadalafil 20 mg once daily and increase to tadalafil 40 mg once daily based on tolerability. *In Patients on Tadalafil who Require EVG/c:* • Stop tadalafil ≥24 hours before EVG/c initiation. Seven days after EVG/c initiation, restart tadalafil at 20 mg once daily, and increase to tadalafil 40 mg once daily based on tolerability.
Vardenafil	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ vardenafil expected	Start with vardenafil 2.5 mg every 72 hours and monitor for adverse effects of vardenafil.
Sedative/Hypnotics			
Clonazepam, Clorazepate, Diazepam, Estazolam, Flurazepam	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	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	BIC, RAL	↔ expected	No dose adjustment necessary.
	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 >1 dose is administered.
Suvorexant	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ suvorexant expected	**Coadministration is not recommended.**
Zolpidem	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ zolpidem expected	Initiate zolpidem at a low dose. Dose reduction may be necessary.

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 14 of 15)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Miscellaneous Drugs			
Calcifediol	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ calcifediol possible	Dose adjustment of calcifediol may be required, and serum 25-hydroxyvitamin D, intact PTH, and serum Ca concentrations should be closely monitored.
Cisapride	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ cisapride expected	**Contraindicated.**
Colchicine	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ colchicine expected	**Do not coadminister in patients with hepatic or renal impairment.** For Treatment of Gout Flares: • Administer colchicine 0.6 mg for 1 dose, followed by colchicine 0.3 mg 1 hour later. Do not repeat dose for at least 3 days. 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.
Enzalutamide	DTG	↓ DTG possible	Monitor for ARV efficacy.
	BIC, EVG/c	↓ BIC, EVG/c expected	**Contraindicated.**
	RAL	↔ expected	No dose adjustment necessary.
Ergot Derivatives	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ dihydroergotamine, ergotamine, methylergonovine expected	**Contraindicated.**
Dronabinol	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ dronabinol possible	Monitor for dronabinol-related adverse effects.
Eluxadoline	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ eluxadoline possible	Monitor for eluxadoline-related adverse effects.
Flibanserin	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ flibanserin expected	**Contraindicated.**
Mitotane	BIC, EVG/c	↓ BIC and ↓ EVG/c expected	**Contraindicated.**
	DTG	↓ DTG possible	Monitor for ARV efficacy.
	RAL	↔ expected	No dose adjustment necessary.

Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated October 25, 2018; last reviewed October 25, 2018) (page 15 of 15)

Concomitant Drug Class/Name	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Miscellaneous Drugs, continued			
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.	BIC	↔ BIC AUC if given simultaneously with Fe or Ca and food BIC AUC ↓ 33% if given simultaneously with $CaCO_3$ under fasting conditions BIC AUC ↓ 63% if given simultaneously with Fe under fasting conditions	With Supplements that Contain Ca or Fe: • BIC and supplements containing Ca or Fe can be taken together with food. **Do not coadminister BIC under fasting conditions simultaneously with, or 2 hours after, supplements containing Ca or Fe.**
	DTG	DTG AUC ↓ 39% if given simultaneously with calcium carbonate under fasting conditions DTG AUC ↓ 54% if given simultaneously with Fe under fasting conditions ↔ DTG when administered with Ca or Fe supplement simultaneously with food	With Supplements That Contain Ca or Fe: • DTG and supplements containing Ca or Fe can be taken together with food; alternately, administer DTG at least 2 hours before or at least 6 hours after supplement. **Do not coadminister DTG under fasting conditions simultaneously with, or 2 hours after, supplements containing Ca or Fe.**
	EVG/c, RAL	↓ INSTI possible	If coadministration is necessary, give INSTI at least 2 hours before or at least 6 hours after supplements containing polyvalent cations, including but not limited to the following products: cation-containing laxatives; Fe, Ca, or Mg supplements; and sucralfate. Monitor for virologic efficacy. Many oral multivitamins also contain varying amounts of polyvalent cations; the extent and significance of chelation is unknown.
Salmeterol	BIC, DTG, RAL	↔ expected	No dose adjustment necessary.
	EVG/c	↑ salmeterol possible	**Do not coadminister**, due to potential increased risk of salmeterol-associated cardiovascular events.

Key to Symbols:

↑ = increase

↓ = decrease

↔ = no change

Key to Acronyms: Al = aluminum; ART = antiretroviral therapy; ARV = antiretroviral; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; BID = twice daily; Ca = calcium; $CaCO_3$ = calcium carbonate; CCB = calcium channel blocker; C_{max} = maximum plasma concentration; C_{min} = minimum plasma concentration; COBI = cobicistat; CrCl = creatinine clearance; CYP = cytochrome P; DTG = dolutegravir; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; Fe = iron; FTC = emtricitabine; INR= international normalized ratio; INSTI = integrase strand transfer inhibitor; Mg = magnesium; PAH = pulmonary arterial hypertension; PI = protease inhibitor; PK = pharmacokinetic; PTH = parathyroid hormone; RAL = raltegravir; RTV = ritonavir; SSRI = selective serotonin reuptake inhibitors; TAF = tenofovir alafenamide; TCA = tricyclic antidepressants; TDF = tenofovir disoproxil fumarate; TDM = therapeutic drug monitoring; Zn = zinc

Table 21e. Drug Interactions between CCR5 Antagonist (Maraviroc) and Other Drugs (Including Antiretroviral Agents) (Last updated October 25, 2018; last reviewed October 25, 2018) (page 1 of 3)

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

Concomitant Drug Class/ Name	CCR5 Antagonist	Effect on CCR5 Antagonist and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
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 dose adjustment is necessary. 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 dose adjustment necessary.
Dasabuvir plus Ombitasvir/Paritaprevir/ RTV	MVC	↑ MVC expected	**Do not coadminister.**
Elbasvir/Grazoprevir	MVC	↔ MVC expected	No dose adjustment necessary.
Ledipasvir/Sofosbuvir	MVC	↔ MVC expected	No dose adjustment necessary.
Glecaprevir/Pibrentasvir	MVC	↔ MVC expected	No dose adjustment necessary.
Simeprevir	MVC	↔ MVC expected	No dose adjustment necessary.
Sofosbuvir	MVC	↔ MVC expected	No dose adjustment necessary.
Sofosbuvir/Velpatasvir	MVC	↔ MVC expected	No dose adjustment necessary.

Table 21e. Drug Interactions between CCR5 Antagonist (Maraviroc) and Other Drugs (Including Antiretroviral Agents) (Last updated October 25, 2018; last reviewed October 25, 2018) (page 2 of 3)

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

Table 21e. Drug Interactions between CCR5 Antagonist (Maraviroc) and Other Drugs (Including Antiretroviral Agents) (Last updated October 25, 2018; last reviewed October 25, 2018) (page 3 of 3)

Concomitant Drug Class/ Name	CCR5 Antagonist	Effect on CCR5 Antagonist and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
PIs, continued			
DRV/c **or** **DRV/r**	MVC	With (DRV/r 600 mg/100 mg) BID: • MVC AUC ↑ 305% With (DRV/r 600 mg/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/r 500 mg/200 mg) BID: • ↔ MVC AUC	No dose adjustment necessary.

Key to Symbols:

↑ = increase

↓ = decrease

↔ = no change

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

Table 22a. Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018) (page 1 of 2)

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

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

Table 22a. Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018) (page 2 of 2)

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

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

[b] DRV concentration was compared to a historic control.

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

Key to Symbols:

↑ = increase

↓ = decrease

↔ = no change

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

Table 22b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018) (page 1 of 3)

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

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
NNRTIs					
DOR	**PK Data**	↔ DOR, BIC expected	↔ DOR DTG AUC ↑ 36% and C_{min} ↑ 27%	↑ DOR expected ↔ EVG	↔ DOR, RAL expected
	Dose	Standard doses	Standard doses	Standard doses	Standard doses
EFV	**PK Data**	↓ BIC expected	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	**Do not coadminister.**	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**	↓ BIC expected	ETR 200 mg BID plus DTG 50 mg Once Daily: • DTG AUC ↓ 71% and C_{min} ↓ 88% ETR 200 mg BID with (DRV 600 mg plus RTV 100 mg) BID and DTG 50 mg Once Daily: • DTG AUC ↓ 25% and C_{min} ↓ 37% ETR 200 mg BID with (LPV 400 mg plus RTV 100 mg) BID and DTG 50 mg Once Daily: • DTG AUC ↑ 11% and C_{min} ↑ 28%	↑ or ↓ EVG, COBI, ETR possible	ETR 200 mg BID plus RAL 400 mg BID: • ETR C_{min} ↑ 17% • RAL C_{min} ↓ 34%

Table 22b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018) (page 2 of 3)

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
NNRTIs, continued					
ETR, continued	**Dose**	**Do not coadminister.**	**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 Resistancea 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**	↓ BIC expected	With DTG 50 mg Once Daily: • DTG AUC ↓ 19% and C_{min} ↓ 34%	↑ or ↓ EVG, COBI, NVP possible	No data
	Dose	**Do not coadminister.**	Standard doses	**Do not coadminister.**	Standard doses
RPV	**PK Data**	No 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	Standard doses	**Do not coadminister.**	Standard doses
PIs					
ATV/c	**PK Data**	BIC AUC ↑ 305%	No data	No data	No data
	Dose	**Do not coadminister.**	Standard doses	**Do not coadminister.**	Standard doses
ATV +/- RTV	**PK Data**	BIC AUC ↑ 310%	Unboosted ATV plus DTG 30 mg Once Daily: • DTG AUC ↑ 91% and C_{min} ↑ 180% (ATV 300 mg plus RTV 100 mg) Once Daily plus 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 plus RTV 100 mg) Once Daily: • RAL AUC ↑ 41%
	Dose	**Do not coadminister.**	Standard doses	**Do not coadminister.**	Standard doses
DRV/c	**PK Data**	BIC AUC ↑ 74%	DRV/c plus DTG Once Daily: • ↔ DTG, DRV, COBI DTG 50 mg Once Daily and DRV/r Once Daily Switched to DRV/c: • DTG C_{min} ↑ 100%	DRV/c plus EVG/c: • ↓ EVG possible	No data
	Dose	Standard doses	Standard doses	**Do not coadminister.**	Standard doses

Table 22b. Interactions between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors (Last updated October 25, 2018; last reviewed October 25, 2018) (page 3 of 3)

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
PIs, continued					
DRV/r	**PK Data**	No data	(DRV 600 mg plus RTV 100 mg) BID with DTG 30 mg Once Daily: • DTG AUC ↓ 22% and C_{min} ↓ 38%	↑ or ↓ EVG, COBI, DRV possible	With (DRV 600 mg plus RTV 100 mg) BID: • RAL AUC ↓ 29% and C_{min} ↑ 38%
	Dose	Standard doses	Standard doses	**Do not coadminister.**	Standard doses
LPV/r	**PK Data**	No data	With (LPV 400 mg plus RTV 100 mg) BID and DTG 30 mg Once Daily: • ↔ DTG	↑ or ↓ EVG, COBI, LPV possible RTV and COBI have similar effects on CYP3A.	↓ RAL ↔ LPV/r
	Dose	**Consider alternative combination.**	Standard doses	**Do not coadminister.**	Standard doses
TPV/r	**PK Data**	↓ BIC possible	With (TPV 500 mg plus RTV 200 mg) BID and DTG 50 mg Once Daily: • DTG AUC ↓ 59% and C_{min} ↓ 76%	↑ or ↓ EVG, COBI, TPV possible RTV and COBI have similar effects on CYP3A.	With (TPV 500 mg plus RTV 200 mg) BID and RAL 400 mg BID: • RAL AUC ↓ 24% and C_{min} ↓ 55%
	Dose	**Do not coadminister.**	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.**

[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; BIC = bictegravir; BID = twice daily; C_{min} = minimum plasma concentration; COBI = cobicistat; CYP = cytochrome P; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; INSTI = integrase strand transfer inhibitor; LPV = lopinavir; LPV/r = lopinavir/ritonavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PK = pharmacokinetic; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; TPV = tipranavir; TPV/r = tipranavir/ritonavir

Appendix B, Table 1. Coformulated Single-Tablet Regimens (Last updated July 10, 2019; last reviewed July 10, 2019)

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

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

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

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

Appendix B, Table 2. Nucleoside Reverse Transcriptase Inhibitor-Based, Fixed-Dose Combination Tablets for Use as Part of an Antiretroviral Regimen (Last updated July 10, 2019; last reviewed July 10, 2019)

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

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

Trade Name (Abbreviations)	ARV Drugs Included in the FDC Tablet	Dosing Recommendation[a]
TAF or TDF plus an NRTI		
Descovy (TAF/FTC)	Tenofovir alafenamide 25 mg/emtricitabine 200 mg	One tablet once daily
Cimduo (TDF/3TC)	Tenofovir disoproxil fumarate 300 mg/lamivudine 300 mg	One tablet once daily
Temixys (TDF/3TC)	Tenofovir disoproxil fumarate 300 mg/lamivudine 300 mg	One tablet once daily
Truvada (TDF/FTC)	Tenofovir disoproxil fumarate 300 mg/emtricitabine 200 mg	One tablet once daily
Other NRTI-Based FDC Tablets		
Epzicom (ABC/3TC) **Note:** Generic is available.	Abacavir 600 mg/lamivudine 300 mg	One tablet once daily
Combivir (ZDV/3TC) **Note:** Generic is available.	Zidovudine 300 mg/lamivudine 150 mg	One tablet twice daily

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

Key: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; FDA = Food and Drug Administration; FDC = fixed-dose combination; FTC = emtricitabine; NRTI = nucleoside reverse transcriptase inhibitor; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; ZDV = zidovudine

Appendix B, Table 3. Characteristics of Nucleoside Reverse Transcriptase Inhibitors (Last updated July 10, 2019; last reviewed July 10, 2019) (page 1 of 4)

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum/ Intracellular Half-Lives	Adverse Events[b]
Abacavir (ABC) *Ziagen* **Note:** Generic tablet formulation is available.	**Ziagen:** • 300 mg tablet • 20 mg/mL oral solution **FDC Tablets that Contain ABC:**[c] • Epzicom (ABC/3TC) • Trizivir (ABC/ZDV/3TC) Also available as part of the STR Triumeq (DTG/ABC/3TC)[c]	**Ziagen:** • ABC 600 mg once daily, *or* • ABC 300 mg twice daily See Appendix B, Tables 1 and 2 for dosing information for FDC tablets that contain ABC.	Metabolized by alcohol dehydrogenase and glucuronyl transferase Renal excretion of metabolites: 82% Dose adjustment is recommended in patients with hepatic insufficiency (see Appendix B, Table 10).	1.5 hours/12–26 hours	Patients who test positive for HLA-B*5701 are at the highest risk of experiencing HSRs. HLA screening should be done before initiating ABC. For patients with a history of HSRs, re-challenge **is not recommended**. Symptoms of HSRs may include fever, rash, nausea, vomiting, diarrhea, abdominal pain, malaise, fatigue, or respiratory symptoms (e.g., sore throat, cough, or shortness of breath). Some cohort studies suggest an increased risk of MI with recent or current use of ABC, but this risk is not substantiated in other studies.
Didanosine (ddI) *Videx* *Videx EC* **Note:** Generic delayed-release capsules are available; the dose for these is the same as for Videx EC.	**Videx EC:** • 125, 200, 250, and 400 mg capsules **Videx:** • 10 mg/mL oral solution	*Body Weight ≥60 kg* Without TDF: • ddI 400 mg once daily With TDF: • ddI 250 mg once daily *Body Weight <60 kg* Without TDF: • ddI 250 mg once daily With TDF: • ddI 200 mg once daily Take ddI a half an hour before or 2 hours after a meal. Oral solution should be administered twice daily, with the total daily dose divided into two doses.	Renal excretion: 50% Dose adjustment is recommended in patients with renal insufficiency (see Appendix B, Table 10).	1.5 hours/>20 hours	Pancreatitis Peripheral neuropathy Retinal changes, optic neuritis Lactic acidosis with hepatic steatosis with or without pancreatitis (this is a 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 an 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 3. Characteristics of Nucleoside Reverse Transcriptase Inhibitors (Last updated July 10, 2019; last reviewed July 10, 2019) (page 2 of 4)

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum/ Intracellular Half-Lives	Adverse Events[b]
Emtricitabine (FTC) *Emtriva*	**Emtriva:** • 200 mg hard gelatin capsule • 10 mg/mL oral solution **FDC Tablets that Contain FTC:**[c] • Descovy (TAF/FTC) • Truvada (TDF/FTC) **STRs that Contain FTC:**[d] • Atripla (EFV/TDF/FTC) • Biktarvy (BIC/TAF/FTC) • Complera (RPV/TDF/FTC) • Genvoya (EVG/c/TAF/FTC) • Odefsey (RPV/TAF/FTC) • Stribild (EVG/c/TDF/FTC) • Symtuza (DRV/c/TAF/FTC)	**Emtriva** *Capsule:* • FTC 200 mg once daily *Oral Solution:* • FTC 240 mg (24 mL) once daily See Appendix B, Tables 1 and 2 for dosing information for FDC tablets that contain FTC.	Renal excretion: 86% Dose adjustment is recommended in patients with renal insufficiency (see Appendix B, Table 10).	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.
Lamivudine (3TC) *Epivir* **Note:** Generic is available.	**Epivir:** • 150 and 300 mg tablets • 10 mg/mL oral solution **FDC Tablets that Contain 3TC:**[c] • Cimduo (TDF/3TC) • Combivir (ZDV/3TC) • Epzicom (ABC/3TC) • Temixys (TDF/3TC) • Trizivir (ABC/ZDV/3TC) **STRs that Contain 3TC:**[d] • Delstrigo (DOR/TDF/3TC) • Dovato (DTG/3TC) • Symfi (EFV 600 mg/TDF/3TC) • Symfi Lo (EFV 400 mg/TDF/3TC) • Triumeq (DTG/ABC/3TC)	**Epivir:** • 3TC 300 mg once daily, *or* • 3TC 150 mg twice daily See Appendix B, Tables 1 and 2 for dosing information for FDC tablets that contain 3TC.	Renal excretion: 70% Dose adjustment is recommended in patients with renal insufficiency (see Appendix B, Table 10).	5–7 hours/ 18–22 hours	Minimal toxicity Severe acute exacerbation of hepatitis may occur in patients with HBV/HIV coinfection who discontinue 3TC.

Appendix B, Table 3. Characteristics of Nucleoside Reverse Transcriptase Inhibitors (Last updated July 10, 2019; last reviewed July 10, 2019) (page 3 of 4)

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum/ Intracellular Half-Lives	Adverse Events[b]
Stavudine (d4T) *Zerit* **Note:** Generic is available.	**Zerit:** • 15, 20, 30, and 40 mg capsules • 1 mg/mL oral solution	*Body Weight ≥60 kg:* • d4T 40 mg twice daily *Body Weight <60 kg:* • d4T 30 mg twice daily WHO recommends 30-mg, twice-daily dose regardless of body weight.	Renal excretion: 50% Dose adjustment is recommended in patients with renal insufficiency (see Appendix B, Table 10).	1 hour/7.5 hours	Peripheral neuropathy Lipoatrophy Pancreatitis Lactic acidosis/severe hepatomegaly with hepatic steatosis (this is a rare, but potentially life-threatening, toxicity) Hyperlipidemia Insulin resistance/diabetes mellitus Rapidly progressive ascending neuromuscular weakness (rare)
Tenofovir Alafenamide (TAF) *Vemlidy* **Note:** Vemlidy is available as a 25-mg tablet for the treatment of HBV.	**STRs that Contain TAF:**[d] • Biktarvy (BIC/TAF/FTC) • Genvoya (EVG/c/TAF/FTC) • Odefsey (RPV/TAF/FTC) • Symtuza (DRV/c/TAF/FTC) Also available as part of the FDC tablet Descovy (TAF/FTC)[c]	See Appendix B, Tables 1 and 2 for dosing information for FDC tablets that contain TAF.	Metabolized by cathepsin A. **Not recommended** in patients with CrCl <30 mL/min.	0.5 hours/150–180 hours	Renal insufficiency, Fanconi syndrome, and proximal renal tubulopathy are less likely to occur with TAF than with TDF. Osteomalacia and decrease in bone mineral density are less likely to occur with TAF than with TDF. Severe acute exacerbation of hepatitis may occur in patients with HBV/HIV coinfection who discontinue TAF. Diarrhea, nausea, headache
Tenofovir Disoproxil Fumarate (TDF) *Viread* **Note:** Generic is available.	**Viread:** • 150, 200, 250, and 300 mg tablets • 40 mg/g oral powder **Generic:** • 300 mg tablet **FDC Tablets that Contain TDF:**[c] • Cimduo (TDF/3TC) • Temixys (TDF/3TC) • Truvada (TDF/FTC) **STRs that Contain TDF:**[d] • Atripla (EFV/TDF/FTC) • Complera (RPV/TDF/FTC) • Delstrigo (DOR/TDF/3TC) • Stribild (EVG/c/TDF/FTC) • Symfi (EFV 600 mg/TDF/3TC) • Symfi Lo (EFV 400 mg/TDF/3TC)	Viread: • TDF 300 mg once daily, *or* • 7.5 level scoops of oral powder once daily (dosing scoop dispensed with each bottle; one level scoop contains 1 g of oral powder). Mix oral powder with 2–4 ounces of a soft food that does not require chewing (e.g., applesauce, yogurt). **Do not mix oral powder with liquid.** See Appendix B, Tables 1 and 2 for dosing information for FDC tablets that contain TDF.	Renal excretion is the primary route of elimination. Dose adjustment is recommended in patients with renal insufficiency (see Appendix B, Table 10).	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, flatulence

Appendix B, Table 3. Characteristics of Nucleoside Reverse Transcriptase Inhibitors (Last updated July 10, 2019; last reviewed July 10, 2019) (page 4 of 4)

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum/ Intracellular Half-Lives	Adverse Events[b]
Zidovudine (ZDV) *Retrovir* **Note:** Generic is available.	**Retrovir:** • 100 mg capsule • 10 mg/mL IV solution • 10 mg/mL oral solution **Generic:** • 300 mg tablet **FDC Tablets that Contain ZDV:**[c] • Combivir (ZDV/3TC) • Trizivir (ABC/ZDV/3TC)	**Retrovir:** • ZDV 300 mg twice daily, *or* • ZDV 200 mg three times a day See Appendix B, Table 2 for dosing information for FDC tablets that contain ZDV.	Metabolized to GAZT Renal excretion of GAZT Dose adjustment is recommended in patients with renal insufficiency (see Appendix B, Table 10).	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 (this is a rare, but potentially life-threatening, toxicity) Hyperlipidemia Insulin resistance/diabetes mellitus Lipoatrophy Myopathy

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

[b] Also see Table 17.

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

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

Key: 3TC = lamivudine; ABC = abacavir; BIC = bictegravir; c = cobicistat; CrCl = creatinine clearance; d4T = stavudine; ddI = didanosine; DOR = doravirine; DRV = darunavir; DTG = dolutegravir; EC = enteric coated; EFV = efavirenz; EVG = elvitegravir; FDC = fixed-dose combination; FTC = emtricitabine; GAZT = azidothymidine glucuronide; HBV = hepatitis B virus; HLA = human leukocyte antigen; HSR = hypersensitivity reaction; IV = intravenous; MI = myocardial infarction; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; WHO = World Health Organization; ZDV = zidovudine

Appendix B, Table 4. Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors (Last updated July 10, 2019; last reviewed July 10, 2019) (page 1 of 2)

Generic Name (Abbreviations) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum Half-Life	Adverse Events[b]
Doravirine (DOR) *Pifeltro*	**Pifeltro:** • 100 mg tablet Also available as part of the STR Delstrigo (DOR/TDF/3TC)[c]	**Pifeltro:** • One tablet once daily See Appendix B, Table 1 for dosing information for Delstrigo.	CYP3A4/5 substrate	15 hours	Nausea Dizziness Abnormal dreams
Efavirenz (EFV) *Sustiva* **Note:** Generic is available.	**Sustiva:** • 50 and 200 mg capsules • 600 mg tablet **Generic:** • 600 mg tablet **STRs that Contain EFV:**[c] • Atripla (EFV/TDF/FTC) • Symfi (EFV 600 mg/TDF/3TC) • Symfi Lo (EFV 400 mg/TDF/3TC)	**Sustiva:** • EFV 600 mg once daily, at or before bedtime Take on an empty stomach to reduce side effects See Appendix B, Table 1 for dosing information for STRs that contain EFV.	Metabolized by CYP2B6 (primary), 3A4, and 2A6 CYP3A4 mixed inducer/inhibitor (more an inducer than an inhibitor) CYP2B6 and 2C19 inducer	40–55 hours	Rash[d] Neuropsychiatric symptoms[e] Serum transaminase elevations Hyperlipidemia Use of EFV may lead to false-positive results with some cannabinoid and benzodiazepine screening assays QT interval prolongation
Etravirine (ETR) *Intelence*	**Intelence:** • 25, 100, and 200 mg tablets	**Intelence:** • ETR 200 mg twice daily Take following a meal.	CYP3A4, 2C9, and 2C19 substrate CYP3A4 inducer CYP2C9 and 2C19 inhibitor	41 hours	Rash, including Stevens-Johnson syndrome[d] HSRs, characterized by rash, constitutional findings, and sometimes organ dysfunction (including hepatic failure), have been reported. Nausea

Appendix B, Table 4. Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors (Last updated July 10, 2019; last reviewed July 10, 2019) (page 2 of 2)

Generic Name (Abbreviations) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum Half-Life	Adverse Events[b]
Nevirapine (NVP) *Viramune* or *Viramune XR* **Note:** Generic 200-mg tablets and oral suspension are available.	**Viramune:** • 200 mg tablet • 50 mg/5 mL oral suspension **Viramune XR:** • 400 mg tablet	**Viramune:** • NVP 200 mg once daily for 14 days (lead-in period); thereafter, NVP 200 mg twice daily, *or* • NVP 400 mg (Viramune XR tablet) once daily Take without regard to meals. Repeat lead-in period if therapy is discontinued for >7 days. In patients who develop mild-to-moderate rash without constitutional symptoms, continue lead-in period until rash resolves, but do not administer for longer than 28 days total.	CYP450 substrate CYP3A4 and 2B6 inducer **Contraindicated** in patients with moderate to severe hepatic impairment. Dose adjustment is recommended in patients on hemodialysis (see Appendix B, Table 10).	25–30 hours	Rash, including Stevens-Johnson syndrome[d] **Symptomatic Hepatitis:** • Symptomatic hepatitis, including fatal hepatic necrosis, has been reported. • Rash has been reported in approximately 50% of cases. • Symptomatic hepatitis occurs at a significantly higher frequency in ARV-naive female patients with pre-NVP CD4 counts >250 cells/mm^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.
Rilpivirine (RPV) *Edurant*	**Edurant:** • 25 mg tablet **STRs that Contain RPV:**[c] • Complera (RPV/TDF/FTC) • Juluca (DTG/RPV) • Odefsey (RPV/TAF/FTC)	**Edurant:** • RPV 25 mg once daily Take with a meal. See Appendix B, Table 1 for dosing information for STRs that contain RPV.	CYP3A4 substrate	50 hours	Rash[d] Depression, insomnia, headache Hepatotoxicity QT interval prolongation

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

[b] Also see Table 17.

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

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

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

Key: 3TC = lamivudine; ARV = antiretroviral; CD4 = CD4 T lymphocyte; CYP = cytochrome P; DOR = doravirine; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; FDC = fixed-dose combination; FTC = emtricitabine; HSR = hypersensitivity reaction; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; XR = extended release

Appendix B, Table 5. Characteristics of Protease Inhibitors (Last updated July 10, 2019; last reviewed July 10, 2019) (page 1 of 6)

Generic Name (Abbreviations) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum Half-Life	Adverse Events[b]
Atazanavir (ATV) *Reyataz* (ATV/c) *Evotaz* **Note:** Generic capsule formulations of ATV are available.	**Reyataz:** • 150, 200, and 300 mg capsules • 50 mg single packet oral powder **Evotaz:** • ATV 300 mg/ COBI 150 mg tablet	**Reyataz** *In ARV-Naive Patients:* • (ATV 300 mg plus RTV 100 mg) once daily; *or* • ATV 400 mg once daily • Take with food. *With TDF or in ARV-Experienced Patients:* • (ATV 300 mg plus RTV 100 mg) once daily • Unboosted ATV **is not recommended**. • Take with food. *With EFV in ARV-Naive Patients:* • (ATV 400 mg plus RTV 100 mg) once daily • Take with food. **Evotaz:** • One tablet once daily • Take with food. • The use of ATV/c **is not recommended** for patients who are taking TDF and who have with baseline CrCl <70 mL/min (see Appendix B, Table 10 for the equation for calculating CrCl). For dosing recommendations with H2 antagonists and PPIs, refer to Table 21a	**ATV:** • CYP3A4 inhibitor and substrate • Weak CYP2C8 inhibitor • UGT1A1 inhibitor **COBI:** • CYP3A inhibitor and substrate • CYP2D6 inhibitor Dose adjustment is recommended in patients with hepatic insufficiency (see Appendix B, Table 10).	7 hours	Indirect hyperbilirubinemia PR interval prolongation. First degree symptomatic AV block has been reported. Use with caution in patients who have underlying conduction defects or who are on concomitant medications that can cause PR prolongation. Cholelithiasis Nephrolithiasis Renal insufficiency Serum transaminase elevations Hyperlipidemia (especially with RTV boosting) Skin rash Hyperglycemia Fat maldistribution An increase in serum creatinine may occur when ATV is administered with COBI

Appendix B, Table 5. Characteristics of Protease Inhibitors (Last updated July 10, 2019; last reviewed July 10, 2019) (page 2 of 6)

Generic Name (Abbreviations) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum Half-Life	Adverse Events[b]
Darunavir (DRV) *Prezista* (DRV/c) *Prezcobix*	**Prezista:** • 75, 150, 600, and 800 mg tablets • 100 mg/mL oral suspension **Prezcobix:** • DRV 800 mg/ COBI 150 mg tablet Also available as part of the STR Symtuza (DRV/c/ TAF/FTC)	**Prezista** *In ARV-Naive Patients or ARV-Experienced Patients with No DRV Mutations:* • (DRV 800 mg plus RTV 100 mg) once daily • Take with food. *In ARV-Experienced Patients with One or More DRV Resistance Mutations:* • (DRV 600 mg plus RTV 100 mg) twice daily • Take with food. Unboosted DRV **is not recommended**. **Prezcobix:** • One tablet once daily • Take with food. • **Not recommended** for patients with one or more DRV resistance-associated mutations. • Coadministering Prezcobix and TDF **is not recommended** for patients with baseline CrCl <70 mL/ min (see Appendix B, Table 10 for the equation for calculating CrCl). See Appendix B, Table 1 for dosing information for Symtuza.	**DRV:** • CYP3A4 inhibitor and substrate • CYP2C9 inducer **COBI:** • CYP3A inhibitor and substrate • CYP2D6 inhibitor	15 hours when combined with RTV 7 hours when combined with COBI	**Skin Rash:** 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 An increase in serum creatinine may occur when DRV is administered with COBI

Appendix B, Table 5. Characteristics of Protease Inhibitors (Last updated July 10, 2019; last reviewed July 10, 2019) (page 3 of 6)

Generic Name (Abbreviations) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum Half-Life	Adverse Events[b]
Fosamprenavir (FPV, a prodrug of APV) *Lexiva* **Note:** Generic is available.	**Lexiva:** • 700 mg tablet • 50 mg/mL oral suspension	*In ARV-Naive Patients:* • FPV 1,400 mg twice daily, *or* • (FPV 1,400 mg plus RTV 100–200 mg) once daily, *or* • (FPV 700 mg plus RTV 100 mg) twice daily *In PI-Experienced Patients:* • (FPV 700 mg plus RTV 100 mg) twice daily • Once-daily dosing **is not recommended** for these patients *In Patients Taking EFV:* • (FPV 700 mg plus RTV 100 mg) twice daily, *or* • (FPV 1,400 mg plus RTV 300 mg) once daily **Food Restrictions** *Without RTV Tablet:* • Take the FPV tablet without regard to meals. *With RTV Tablet:* • Take the RTV tablet and FPV tablet with meals. *Oral Suspension:* • Take without food.	APV is a CYP3A4 substrate, inhibitor, and inducer. Dose adjustment is recommended in patients with hepatic insufficiency (see Appendix B, Table 10).	7.7 hours (APV)	Skin rash has been reported in 12% to 19% of patients on FPV. FPV has a sulfonamide moiety. Diarrhea, nausea, vomiting Headache Hyperlipidemia Serum transaminase elevation Hyperglycemia Fat maldistribution Possible increase in the frequency of bleeding episodes in patients with hemophilia Nephrolithiasis
Indinavir (IDV) *Crixivan*	**Crixivan:** • 200 and 400 mg capsules	**Crixivan:** • IDV 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 plus RTV 100–200 mg) twice daily • Take without regard to meals. Patients should drink at least 48 ounces of water daily while taking IDV.	CYP3A4 inhibitor and substrate Dose adjustment is recommended in patients with hepatic insufficiency (see Appendix B, Table 10).	1.5–2 hours	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 increase in the frequency of bleeding episodes in patients with hemophilia

Appendix B, Table 5. Characteristics of Protease Inhibitors (Last updated July 10, 2019; last reviewed July 10, 2019) (page 4 of 6)

Generic Name (Abbreviations) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum Half-Life	Adverse Events[b]
Lopinavir/ Ritonavir (LPV/r) *Kaletra* **Note:** LPV is only available as a component of an FDC tablet that also contains RTV.	**Kaletra:** • LPV/r 200 mg/50 mg tablets • LPV/r 100 mg/25 mg tablets • LPV/r 400 mg/100 mg per 5 mL of oral solution. Oral solution contains 42% alcohol.	**Kaletra:** • LPV/r 400 mg/100 mg twice daily, *or* • LPV/r 800 mg/200 mg once daily. However, Once-daily dosing **is not recommended** for patients with three or more LPV-associated mutations, pregnant women, or patients receiving EFV, NVP, FPV, NFV, carbamazepine, phenytoin, or phenobarbital. *With EFV or NVP in PI-Naive or PI-Experienced Patients:* • LPV/r 500 mg/125 mg tablets twice daily (use a combination of two LPV/r 200 mg/50 mg tablets plus one LPV/r 100 mg/25 mg tablet to make a total dose of LPV/r 500 mg/125 mg), *or* • LPV/r 533 mg/133 mg oral solution twice daily **Food Restrictions** *Tablet:* • Take without regard to meals. *Oral Solution:* • Take with food.	CYP3A4 inhibitor and substrate	5–6 hours	GI intolerance, nausea, vomiting, diarrhea Pancreatitis Asthenia Hyperlipidemia (especially hypertriglyceridemia) Serum transaminase elevation Hyperglycemia Insulin resistance/diabetes mellitus Fat maldistribution Possible increase in the frequency of 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*	**Viracept:** • 250 and 625 mg tablets	**Viracept:** • NFV 1,250 mg twice daily, *or* • NFV 750 mg three times a day 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	Diarrhea Hyperlipidemia Hyperglycemia Fat maldistribution Possible increase in the frequency of bleeding episodes in patients with hemophilia Serum transaminase elevation

Appendix B, Table 5. Characteristics of Protease Inhibitors (Last updated July 10, 2019; last reviewed July 10, 2019) (page 5 of 6)

Generic Name (Abbreviations) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum Half-Life	Adverse Events[b]
Ritonavir (RTV) *Norvir* **Note:** Generic is available. Although RTV was initially developed as a PI for HIV treatment, RTV is currently used at a lower dose of 100 mg to 200 mg once or twice daily as a PK enhancer to increase the concentrations of other PIs.	**Norvir:** • 100 mg tablet • 100 mg soft gel capsule • 80 mg/mL oral solution. Oral solution contains 43% alcohol. • 100 mg single packet oral powder Also available as part of the FDC tablet Kaletra (LPV/r)	**As a PK Booster (or Enhancer) for Other PIs:** • RTV 100–400 mg per day in one or two divided doses (refer to other PIs for specific dosing recommendations). **Food Restrictions** *Tablet:* • Take with food. *Capsule and Oral Solution:* • To improve tolerability, take with food if possible.	CYP3A4 > 2D6 substrate Potent CYP3A4 and 2D6 inhibitor Inducer of UGT1A1 and CYPs 1A2, 2C8, 2C9, and 2C19	3–5 hours	GI intolerance, nausea, vomiting, diarrhea Paresthesia (circumoral and extremities) Hyperlipidemia (especially hypertriglyceridemia) Hepatitis Asthenia Taste perversion Hyperglycemia Fat maldistribution Possible increase in the frequency of bleeding episodes in patients with hemophilia
Saquinavir (SQV) *Invirase*	**Invirase:** • 500 mg tablet • 200 mg capsule	**Invirase:** • (SQV 1,000 mg plus RTV 100 mg) twice daily Unboosted SQV **is not recommended**. Take with meals or within 2 hours after a meal.	CYP3A4 substrate	1–2 hours	GI intolerance, nausea, and diarrhea Headache Serum transaminase elevation Hyperlipidemia Hyperglycemia Fat maldistribution Possible increase in the frequency of bleeding episodes in patients with hemophilia PR interval prolongation QT interval prolongation. Cases of Torsades de Pointes have been reported. Patients with pre-SQV QT intervals >450 msec should not receive SQV.

Appendix B, Table 5. Characteristics of Protease Inhibitors (Last updated July 10, 2019; last reviewed July 10, 2019) (page 6 of 6)

Generic Name (Abbreviations) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum Half-Life	Adverse Events[b]
Tipranavir (TPV) *Aptivus*	**Aptivus:** • 250 mg capsule • 100 mg/mL oral solution	**Aptivus:** • (TPV 500 mg plus RTV 200 mg) twice daily • Unboosted TPV **is not recommended**. **Food Restrictions** *With RTV Tablets:* • Take with meals. *With RTV Capsules or Solution:* • Take without regard to meals.	CYP3A4 inducer and substrate CYP2D6 inhibitor; CYP3A4, 1A2, and 2C19 inducer Net effect of combining TPV and RTV is a CYP3A4 and 2D6 inhibitor	6 hours after single dose of TPV/r	Hepatotoxicity. Clinical hepatitis (including hepatic decompensation and hepatitis-associated fatalities) has been reported; monitor patients closely, especially those with underlying liver diseases. Skin rash. 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 increase in the frequency of bleeding episodes in patients with hemophilia

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

[b] Also see Table 17.

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

Appendix B, Table 6. Characteristics of Integrase Strand Transfer Inhibitors (Last updated July 10, 2019; last reviewed July 10, 2019) (page 1 of 2)

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathways	Serum Half-Life	Adverse Events[b]
Bictegravir (BIC)	BIC is only available as part of the STR Biktarvy (BIC/TAF/FTC).[c]	**Biktarvy:** • One tablet once daily	CYP3A4 substrate UGT1A1-mediated glucuronidation	~17 hours	Diarrhea Nausea Headache
Dolutegravir (DTG) *Tivicay*	**Tivicay:** • 50 mg tablet **STRs that Contain DTG:**[c] • Dovato (DTG/3TC) • Juluca (DTG/RPV) • Triumeq (DTG/ABC/3TC)	*In ARV-Naive or ARV-Experienced, INSTI-Naive Patients:* • DTG 50 mg once daily *In ARV-Naive or ARV-Experienced, INSTI-Naive Patients when Coadministered with EFV, FPV/r, TPV/r, or Rifampin:* • DTG 50 mg twice daily *INSTI-Experienced Patients with Certain INSTI Mutations (See Product Label) or with Clinically Suspected INSTI Resistance:* • DTG 50 mg twice daily See Appendix B, Table 1 for dosing information for STRs that contain DTG.	UGT1A1-mediated glucuronidation Minor substrate of CYP3A4	~14 hours	Insomnia Headache Depression and suicidal ideation (rare; usually occurs in patients with pre-existing psychiatric conditions) Weight gain Hepatotoxicity Preliminary data suggest an increased rate of neural tube defects in infants born to mothers who were taking DTG at the time of conception. HSRs, including rash, constitutional symptoms, and organ dysfunction (including liver injury), have been reported.
Elvitegravir (EVG) **Note:** EVG is only available as a component of an FDC tablet that also contains COBI, FTC, and either TDF or TAF.	**STRs that Contain EVG:**[c] • Genvoya (EVG/c/TAF/FTC) • Stribild (EVG/c/TDF/FTC)	**Genvoya:** • One tablet once daily with food • See Appendix B, Table 10 for dosing recommendations in persons with renal insufficiency. **Stribild:** • One tablet once daily with food • **Not recommended** for patients with baseline CrCl <70 mL/min (see Appendix B, Table 10 for the equation for calculating CrCl).	**EVG:** • CYP3A and UGT1A1/3 substrate **COBI:** • CYP3A inhibitor and substrate • CYP2D6 inhibitor	~13 hours (EVG/c)	Nausea Diarrhea Depression and suicidal ideation (rare; usually occurs in patients with pre-existing psychiatric conditions)

Appendix B, Table 6. Characteristics of Integrase Strand Transfer Inhibitors (Last updated July 10, 2019; last reviewed July 10, 2019) (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*	**Isentress:** • 400 mg tablet • 25 and 100 mg chewable tablets • 100 mg single packet for oral suspension **Isentress HD:** • 600 mg tablet	**Isentress** *In ARV-Naive Patients or ARV-Experienced Patients:* • 400 mg twice daily *With Rifampin:* • 800 mg twice daily **Isentress HD** *In ARV-Naive or ARV-Experienced Patients with Virologic Suppression on a Regimen of RAL 400 mg Twice Daily:* • 1,200 mg (two 600-mg tablets) once daily *With Rifampin:* • **Not recommended**	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 occurs in patients with pre-existing psychiatric conditions)

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

[b] Also see Table 17.

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

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

Appendix B, Table 7. Characteristics of the Fusion Inhibitor (Lasted updated January 29, 2008; last reviewed July 10, 2019)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendation	Serum Half-Life	Elimination	Adverse Events[a]
Enfuvirtide (T-20) *Fuzeon*	**Fuzeon:** • Injectable; supplied as lyophilized powder. • Each vial contains 108 mg of T-20; reconstitute with 1.1 mL of sterile water for injection for delivery of approximately 90 mg/1 mL. • Refer to prescribing information for storage instruction.	**Fuzeon:** • T-20 90 mg/1 mL SQ twice daily	3.8 hours	Expected to undergo catabolism to its constituent amino acids, with subsequent recycling of the amino acids in the body pool	Local injection site reactions (e.g., pain, erythema, induration, nodules and cysts, pruritus, ecchymosis) in almost 100% of patients Increased incidence of bacterial pneumonia HSR occurs in <1% of patients. Symptoms may include rash, fever, nausea, vomiting, chills, rigors, hypotension, or elevated serum transaminases. **Re-challenge is not recommended.**

[a] Also see Table 17.

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

Appendix B, Table 8. Characteristics of the CCR5 Antagonist (Lasted updated March 27, 2012; last reviewed July 10, 2019)

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations[a]	Serum Half-Life	Elimination/ Metabolic Pathway	Adverse Events[b]
Maraviroc (MVC) *Selzentry*	**Selzentry:** • 150 and 300 mg tablets	**Selzentry:** • MVC 150 mg twice daily when given with drugs that are strong CYP3A inhibitors (with or without CYP3A inducers), including PIs (except TPV/r) • MVC 300 mg twice daily when given with NRTIs, T-20, TPV/r, NVP, RAL, and other drugs that are not strong CYP3A inhibitors or inducers • MVC 600 mg twice daily when given with drugs that are CYP3A inducers, including EFV, ETR, etc. (without a CYP3A inhibitor) Take MVC 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 dose adjustments in patients with hepatic insufficiency, see Appendix B, Table 10.

[b] Also see Table 17.

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

Appendix B, Table 9. Characteristics of the CD4 Post-Attachment Inhibitor (Last updated July 10, 2019; last reviewed July 10, 2019)

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

Key: IBA = ibalizumab; IV = intravenous

Appendix B, Table 10. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency (Last updated July 10, 2019; last reviewed July 10, 2019) (page 1 of 7)

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

Generic Name (Abbreviations) *Trade Name*	Usual Daily Dose[a]	Dosing in Patients with Renal Insufficiency[b]	Dosing in Patients with Hepatic Impairment
NRTIs Stribild **should not be initiated** in patients with CrCl <70 mL/min. The following FDC tablets **are not recommended** in patients with CrCl <50 mL/min: Atripla, Combivir, Complera, Delstrigo, Dovato, Epzicom, Triumeq, or Trizivir. Biktarvy, Descovy, Odefsey, Symtuza, and Truvada **are not recommended** in patients with CrCl <30 mL/min.			
Abacavir (ABC) *Ziagen*	ABC 300 mg PO twice daily *or* ABC 600 mg PO once daily	No dose adjustment necessary.	*Child-Pugh Class A:* ABC 200 mg PO twice daily (use oral solution) *Child-Pugh Class B or C:* **Contraindicated**
Didanosine EC (ddI) *Videx EC*	*Body Weight ≥60 kg:* • ddI 400 mg PO once daily *Body Weight <60 kg:* • ddI 250 mg PO once daily	**Once-Daily Dose by Body Weight** **CrCl (mL/min) / ≥60 kg / <60 kg** 30–59 / 200 mg / 125 mg 10–29 / 125 mg / 125 mg <10, HD,[c] or CAPD / 125 mg / 75 mg oral solution	No dose adjustment necessary.
Didanosine Oral Solution (ddI) *Videx*	*Body Weight ≥60 kg:* • ddI 200 mg PO twice daily, *or* • ddI 400 mg PO once daily *Body Weight <60 kg:* • ddI 250 mg PO once daily, *or* • ddI 125 mg PO twice daily	**Once-Daily Dose by Body Weight** **CrCl (mL/min) / ≥60 kg / <60 kg** 30–59 / 200 mg / 150 mg 10–29 / 150 mg / 100 mg <10, HD,[c] or CAPD / 100 mg / 75 mg	No dose adjustment necessary.
Emtricitabine (FTC) *Emtriva*	FTC 200 mg oral capsule once daily *or* FTC 240 mg (24 mL) oral solution once daily	**Dose by Formulation** **CrCl (mL/min) / Capsule / Solution** 30–49 / 200 mg q48h / 120 mg q24h 15–29 / 200 mg q72h / 80 mg q24h <15 or on HD[c] / 200 mg q96h / 60 mg q24h	No dose recommendation.
Lamivudine (3TC) *Epivir*	3TC 300 mg PO once daily *or* 3TC 150 mg PO twice daily	**CrCl (mL/min) / Dose** 30–49 / 150 mg q24h 15–29 / 1 x 150 mg, then 100 mg q24h 5–14 / 1 x 150 mg, then 50 mg q24h <5 or on HD[c] / 1 x 50 mg, then 25 mg q24h	No dose adjustment necessary.

Appendix B, Table 10. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency (Last updated July 10, 2019; last reviewed July 10, 2019) (page 2 of 7)

Generic Name (Abbreviations) *Trade Name*	Usual Daily Dose[a]	Dosing in Patients with Renal Insufficiency[b]	Dosing in Patients with Hepatic Impairment
NRTIs, continued			
Stavudine (d4T) *Zerit*	*Body Weight ≥60 kg:* • d4T 40 mg PO twice daily *Body Weight <60 kg:* • d4T 30 mg PO twice daily	**Dose by Body Weight** **CrCl (mL/min)** / **≥60 kg** / **<60 kg** 26–50 / 20 mg q12h / 15 mg q12h 10–25 or on HD[c] / 20 mg q24h / 15 mg q24h	No dose recommendation.
Tenofovir Alafenamide/ Emtricitabine (TAF/FTC) *Descovy*	TAF for HIV treatment is only available as a component of FDC tablets (i.e., Descovy, Genvoya, Odefsey, Biktarvy, and Symtuza). TAF 10 mg PO daily with EVG/c (Genvoya) or DRV/c (Symtuza) TAF 25 mg PO daily in other FDC tablets	**CrCl (mL/min)** / **Dose** <30 or on HD[c] / **Not recommended**	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No dose recommendation
Tenofovir Disoproxil Fumarate (TDF) *Viread*	TDF 300 mg PO once daily	**CrCl (mL/min)** / **Dose** 30–49 / 300 mg q48h 10–29 / 300 mg twice weekly (q72–96h) <10 and not on HD / No recommendation On HD[c] / 300 mg q7d	No dose adjustment necessary.
Tenofovir Disoproxil Fumarate/ Emtricitabine (TDF/FTC) *Truvada*	One tablet PO once daily	**CrCl (mL/min)** / **Dose** 30–49 / One tablet q48h <30 or on HD / **Not recommended**	No dose recommendation.
Tenofovir Disoproxil Fumarate/ Lamivudine (TDF/3TC) *Cimduo*	One tablet PO once daily	**CrCl (mL/min)** / **Dose** <50 or on HD / **Not recommended**	No dose recommendation.
Zidovudine (ZDV) *Retrovir*	ZDV 300 mg PO twice daily	**CrCl (mL/min)** / **Dose** <15 or on HD[c] / 100 mg three times a day or 300 mg once daily	No dose recommendation.
NNRTIs			
Doravirine (DOR) *Pifeltro*	One tablet PO once daily	No dose adjustment required in mild, moderate, or severe renal impairment. Has not been studied in ESRD or HD.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* Not studied

Appendix B, Table 10. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency (Last updated July 10, 2019; last reviewed July 10, 2019) (page 3 of 7)

Generic Name (Abbreviations) *Trade Name*	Usual Daily Dose[a]	Dosing in Patients with Renal Insufficiency[b]	Dosing in Patients with Hepatic Impairment
NNRTIs, continued			
Doravirine/ Tenofovir Disoproxil Fumarate/ Lamivudine (DOR/TDF/3TC) *Delstrigo*	One tablet PO once daily	**Not recommended** if CrCl <50 mL/min.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* Not studied
Efavirenz (EFV) *Sustiva*	EFV 600 mg PO once daily on an empty stomach, preferably at bedtime	No dose adjustment necessary.	No dose recommendation; use with caution in patients with hepatic impairment.
Efavirenz/ Tenofovir Disoproxil Fumarate/ Emtricitabine (EFV/TDF/FTC) *Atripla*	One tablet once daily on an empty stomach, preferably at bedtime	**Not recommended** if CrCl <50 mL/min. Instead, use the individual drugs and adjust TDF and FTC doses according to CrCl level.	No dose recommendation; use with caution in patients with hepatic impairment.
Efavirenz 600 mg/Tenofovir Disoproxil Fumarate/ Lamivudine (EFV/TDF/3TC) *Symfi*	One tablet once daily on an empty stomach, preferably at bedtime	**Not recommended** if CrCl <50 mL/min or if patient is on HD. Instead, use the individual drugs and adjust TDF and 3TC doses according to CrCl level.	**Not recommended** for patients with moderate or severe hepatic impairment. Use caution in patients with mild hepatic impairment.
Efavirenz 400 mg/Tenofovir Disoproxil Fumarate/ Lamivudine (EFV/TDF/3TC) *Symfi Lo*	One tablet once daily on an empty stomach, preferably at bedtime	**Not recommended** if CrCl <50 mL/min or if patient is on HD. Instead, use the individual drugs and adjust TDF and 3TC doses according to CrCl level.	**Not recommended** for patients with moderate or severe hepatic impairment. Use caution in patients with mild hepatic impairment.
Etravirine (ETR) *Intelence*	ETR 200 mg PO twice daily	No dose adjustment necessary.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No dose recommendation
Nevirapine (NVP) *Viramune* or *Viramune XR*	NVP 200 mg PO twice daily *or* NVP 400 mg PO once daily (using Viramune XR formulation)	No dose adjustment for patients with renal impairment. Patients on HD should receive an additional dose of NVP 200 mg following each dialysis treatment.	*Child-Pugh Class A:* No dose adjustment *Child-Pugh Class B or C:* **Contraindicated**
Rilpivirine (RPV) *Edurant*	RPV 25 mg PO once daily	No dose adjustment necessary.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No dose recommendation

Appendix B, Table 10. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency (Last updated July 10, 2019; last reviewed July 10, 2019) (page 4 of 7)

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

Appendix B, Table 10. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency (Last updated July 10, 2019; last reviewed July 10, 2019) (page 5 of 7)

Generic Name (Abbreviations) *Trade Name*	Usual Daily Dose[a]	Dosing in Patients with Renal Insufficiency[b]	Dosing in Patients with Hepatic Impairment
PIs, continued			
Darunavir/ Cobicistat/ Tenofovir Alafenamide/ Emtricitabine (DRV/c/TAF/FTC) *Symtuza*	One tablet PO once daily	**Not recommended** if CrCl <30 mL/min.	**Not recommended** for patients with severe hepatic impairment.
Fosamprenavir (FPV) *Lexiva*	1,400 mg PO twice daily *or* (FPV 1,400 mg plus RTV 100–200 mg) PO once daily *or* (FPV 700 mg plus RTV 100 mg) PO twice daily	No dose adjustment necessary.	**In PI-Naive Patients Only (without RTV)** *Child-Pugh Score 5–9:* • FPV 700 mg twice daily *Child-Pugh Score 10–15:* • FPV 350 mg twice daily **In PI-Naive or PI-Experienced Patients** *Child-Pugh Score 5–6:* • FPV 700 mg twice daily plus RTV 100 mg once daily *Child-Pugh Score 7–9:* • FPV 450 mg twice daily plus RTV 100 mg once daily *Child-Pugh Score 10–15:* • FPV 300 mg twice daily plus RTV 100 mg once daily
Indinavir (IDV) *Crixivan*	IDV 800 mg PO q8h	No dose adjustment necessary.	*In Patients with Mild-to-Moderate Hepatic Insufficiency Due to Cirrhosis:* IDV 600 mg q8h
Lopinavir/ Ritonavir (LPV/r) *Kaletra*	(LPV/r 400 mg/100 mg) PO twice daily *or* (LPV/r 800 mg/200 mg) PO once daily	Avoid once-daily dosing in patients on HD.	No dose recommendation; use with caution in patients with hepatic impairment.
Nelfinavir (NFV) *Viracept*	NFV 1,250 mg PO twice daily	No dose adjustment necessary.	*In Patients with Mild Hepatic Impairment:* No dose adjustment *In Patients with Moderate-to-Severe Hepatic Impairment:* **Not recommended**
Ritonavir (RTV) *Norvir*	*As a PI-Boosting Agent:* • RTV 100–400 mg per day	No dose adjustment necessary.	Refer to recommendations for the primary PI.
Saquinavir (SQV) *Invirase*	(SQV 1,000 mg plus RTV 100 mg) PO twice daily	No dose adjustment necessary.	*In Patients with Mild-to-Moderate Hepatic Impairment:* Use with caution *In Patients with Severe Hepatic Impairment:* **Contraindicated**

Appendix B, Table 10. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency (Last updated July 10, 2019; last reviewed July 10, 2019) (page 6 of 7)

Generic Name (Abbreviations) *Trade Name*	Usual Daily Dose[a]	Dosing in Patients with Renal Insufficiency[b]	Dosing in Patients with Hepatic Impairment
PIs, continued			
Tipranavir (TPV) *Aptivus*	(TPV 500 mg plus RTV 200 mg) PO twice daily	No dose adjustment necessary.	*Child-Pugh Class A:* Use with caution *Child-Pugh Class B or C:* **Contraindicated**
INSTIs			
Bictegravir/ Tenofovir Alafenamide/ Emtricitabine (BIC/TAF/FTC) *Biktarvy*	One tablet once daily	**Not recommended** for use in patients with CrCl <30 mL/min.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* **Not recommended**
Dolutegravir (DTG) *Tivicay*	DTG 50 mg once daily *or* DTG 50 mg twice daily	No dose adjustment necessary.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* **Not recommended**
Dolutegravir/ Abacavir/ Lamivudine (DTG/ABC/3TC) *Triumeq*	One tablet once daily	Not recommended if CrCl <50 mL/min. Instead, use the individual drugs and adjust 3TC dose according to CrCl.	*Child-Pugh Class A:* Patients with mild hepatic impairment require a dose reduction of ABC. Use the individual drugs instead of the FDC tablet in these patients. *Child-Pugh Class B or C:* **Contraindicated** due to the ABC component
Dolutegravir/ Rilpivirine (DTG/RPV) *Juluca*	One tablet PO once daily with food	No dose adjustment necessary. In patients with CrCl <30 mL/min, monitor closely for adverse effects.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No dose recommendation
Elvitegravir/ Cobicistat/ Tenofovir Alafenamide/ Emtricitabine (EVG/c/TAF/FTC) *Genvoya*	One tablet once daily	*In Patients on Chronic HD:* • One tablet once daily. On dialysis days, administer after dialysis. **Not recommended** in patients with CrCl <30 mL/min or ≤15 mL/min who are not receiving chronic HD.	*In Patients with Mild-to-Moderate Hepatic Insufficiency:* No dose adjustment necessary *In Patients with Severe Hepatic Insufficiency:* **Not recommended**
Elvitegravir/ Cobicistat/ Tenofovir Disoproxil Fumarate/ Emtricitabine (EVG/c/TDF/FTC) *Stribild*	One 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.	*In Patients with Mild-to-Moderate Hepatic Insufficiency:* No dose adjustment necessary *In Patients with Severe Hepatic Insufficiency:* **Not recommended**
Raltegravir (RAL) *Isentress* *Isentress HD*	RAL 400 mg twice daily (using Isentress formulation) *or* RAL 1,200 mg once daily (using Isentress HD formulation only)	No dose adjustment necessary.	*In Patients with Mild-to-Moderate Hepatic Insufficiency:* No dose adjustment necessary *In Patients with Severe Hepatic Insufficiency:* No recommendation

Appendix B, Table 10. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency (Last updated July 10, 2019; last reviewed July 10, 2019) (page 7 of 7)

Generic Name (Abbreviations) *Trade Name*	Usual Daily Dose[a]	Dosing in Patients with Renal Insufficiency[b]	Dosing in Patients with Hepatic Impairment
Fusion Inhibitor			
Enfuvirtide (T-20) *Fuzeon*	T-20 90 mg SQ twice daily	No dose adjustment necessary.	No dose 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 8 for detailed dosing information.	*In Patients with CrCl <30 mL/min or Patients Who Are on HD* Without Potent CYP3A Inhibitors or Inducers: • MVC 300 mg twice daily; reduce to 150 mg twice daily if postural hypotension occurs With Potent CYP3A Inducers or Inhibitors: • **Not recommended**	No dose recommendations. MVC concentrations will likely be increased in patients with hepatic impairment.
CD4 Post-Attachment Inhibitor			
Ibalizumab (IBA) *Trogarzo*	Loading dose of IBA 2,000 mg IV, followed by a maintenance dose of IBA 800 mg IV every 2 weeks	No dose adjustment recommended.	No recommendation.

[a] Refer to Appendix B, Tables 1–9 for additional dosing information.

[b] Including patients who are on CAPD and HD.

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

Key: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; CAPD = chronic ambulatory peritoneal dialysis; COBI = cobicistat; CrCl = creatinine clearance; CYP = cytochrome P; d4T = stavudine; ddI = didanosine; DLV = delavirdine; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DTG = dolutegravir; EC = enteric coated; EFV = efavirenz; ESRD = end stage renal disease; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FDC = fixed-dose combination; FPV = fosamprenavir; FTC = emtricitabine; HD = hemodialysis; IBA = ibalizumab; IDV = indinavir; INSTI = integrase strand transfer inhibitor; IV = intravenous; LPV = lopinavir; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PO = orally; q(n)d = every (n) days; q(n)h = every (n) hours; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQ = subcutaneous; SQV = saquinavir; T-20 = enfuvirtide; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; 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 (34–50 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