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

Developed by the HHS Panel on Antiretroviral Guidelines for Adults and Adolescents—A Working Group of the NIH Office of AIDS Research Advisory Council (OARAC)

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It is emphasized that concepts relevant to HIV management evolve rapidly. The Panels have a mechanism to update recommendations on a regular basis, and the most recent information is available on the Clinicalinfo website (https://clinicalinfo.hiv.gov/).

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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 (ARV) agents for the treatment of HIV in adults and adolescents in the United States.
Panel members	The Panel is composed of approximately 50 voting members who have expertise in HIV care and research and includes at least one representative from each of the following U.S. Department of Health and Human Services (HHS) agencies: Centers for Disease Control and Prevention (CDC), U.S. Food and Drug Administration (FDA), Health Resource and Services Administration (HRSA), and National Institutes of Health (NIH). Approximately two-thirds of the Panel members are nongovernmental scientific members. The Panel also includes four to five community members with knowledge of HIV treatment and care. The U.S. government representatives are appointed by their respective agencies; other Panel members are selected after an open call for nominations. Each member serves on the Panel for a 4-year term, with an option for reappointment for an additional term. See the 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 to manage HIV infection. The latest version of the Financial Disclosure list is available on the Clinicalinfo website.
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 or data available in FDA drug labels. On some occasions, particularly when new information may affect patient safety, unpublished data presented at major conferences or prepared by the FDA and/or manufacturers as warnings to the public may be used as evidence to revise the guidelines.
Recommendation grading	As described in Table 2 below
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) for adults and adolescents with HIV. For a more detailed discussion on the use of ART in children and prepubertal adolescents (those with sexual maturity ratings of 1 to 3), clinicians should refer to the Pediatric Antiretroviral Guidelines. These guidelines also include a brief discussion on the management of persons of childbearing potential and pregnant persons. For more details on the use of ARV drugs during pregnancy, see the Perinatal Guidelines.
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 relating to ARV drugs that may have an impact on the clinical care of people with HIV. In the event of new data of clinical importance, the Panel may post an interim announcement with recommendations on the Clinicalinfo website until the guidelines can be updated with the appropriate changes. Updated guidelines are available on the Clinicalinfo website.

Table 1. Outline of the Guidelines Development Process

Topic	Comment
Public comments	A 2-week public comment period follows the release of the updated guidelines on the Clinicalinfo website. The Panel reviews comments to determine whether additional revisions to the guidelines are indicated. The public also may submit comments to the Panel at any time at HIVinfo@NIH.gov.

Table 2. Rating Scheme for Recommendations

Recommendations in these guidelines are based on scientific evidence and expert opinion. Each recommendation statement includes a letter **(A**, **B**, or **C)** that represents the strength of the recommendation and a Roman numeral **(I**, **II**, or **III)** that represents the quality of the evidence that supports the recommendation (see Table 2 below).

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

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

Laboratory Test	Timepoint or Frequency of Testing								
	Entry Into Care	ART Initiation[b] or Modification	4 to 8 Weeks After ART Initiation or Modification	Every 3 Months	Every 6 Months	Every 12 Months	Treatment Failure	Clinically Indicated	If ART Initiation Is Delayed[c]
HIV Antigen/ Antibody Test	√ If HIV diagnosis has not been confirmed								
CD4 Count	√	√		√[d] If CD4 count is <300 cells/mm^3	√ During the first 2 years of ART, 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 count monitoring is optional.	√	√	√ Every 3–6 months
HIV Viral Load	√	√	√[e]	√[f]	√[f]		√	√	Repeat testing is optional.

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Genotypic Resistance Testing (PR/RT Genes)[g]	√	√					√	√	√
Genotypic Resistance Testing (Integrase Genes)[g]	√ If transmitted INSTI resistance is suspected or if there is a history of CAB-LA use for PrEP	√[f] If transmitted INSTI resistance is suspected or if there is a history of INSTI use					√ If there is a history of INSTI use	√ If there is a history of INSTI use	
Tropism Testing		√ If considering a CCR5 antagonist					√ If considering a CCR5 antagonist, or for patients with virologic failure on a CCR5 antagonist	√	
HLA-B*5701 Testing		√ If considering ABC							

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Hepatitis B Serology (HBsAb, HBsAg, HBcAb total)[h,i,j]	√	In patients not immune to HBV, consider retesting if switching to a regimen that does not contain TDF or TAF.						√ Including before starting HCV DAA	
Hepatitis C Screening (HCV antibody or, if indicated, HCV RNA)[k]	√					√ Repeat HCV screening for at-risk patients[l]		√	
Basic Metabolic Panel[m,n]	√	√	√		√			√	√ Every 6–12 months
ALT, AST, Total Bilirubin	√	√	√		√			√	√ Every 6–12 months
CBC with Differential[o]	√	√		√ When monitoring CD4 count (if required by lab)	√ When monitoring CD4 count (if required by lab)	√ When no longer monitoring CD4 count		√	

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

Laboratory Test	Timepoint or Frequency of Testing								
	Entry Into Care	ART Initiation[b] or Modification	4 to 8 Weeks After ART Initiation or Modification	Every 3 Months	Every 6 Months	Every 12 Months	Treatment Failure	Clinically Indicated	If ART Initiation Is Delayed[c]
Lipid Profile[p]	√		Consider 1–3 months after ARV initiation or modification			√ If normal at baseline but with CV risk		If normal at baseline, every 5 years or if clinically indicated	
Random or Fasting Glucose[q]	√	√					√	√	
Urinalysis[n,r]	√							√ E.g., in patients with CKD or DM	
Pregnancy Test[s]	√	√						√	

[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 Medicine Association of the Infectious Diseases Society of America's (HIVMA/IDSA) Primary Care Guidance for Persons with HIV for other laboratory tests generally recommended for primary health care maintenance of HIV patients.[1]

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

[c] ART is indicated for all people 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] After 2 years of consistently suppressed HIV RNA, less frequent monitoring (e.g., every 6 months) may be considered.

[e] If HIV RNA is detectable at 4–8 weeks, repeat testing every 4–8 weeks until viral load is suppressed to <50 copies/mL. Thereafter, repeat testing every 3–6 months.

[f] For patients on ART, viral load typically is measured every 3–6 months. More frequent monitoring may be considered in individuals having difficulties with ART adherence or at risk for nonadherence. However, for adherent patients with consistently suppressed viral load and stable immunologic status for more than 1 year, monitoring can be extended to 6-month intervals.

[g] Standard genotypic drug-resistance testing in ARV-naive persons should focus on testing for mutations in the PR and RT genes. If transmitted INSTI resistance is a concern, or if a person has a history of INSTI use as PrEP or treatment, or a person presents with viremia while on an INSTI, providers also should test for resistance mutations in the IN gene. In ARV-naive patients who do

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

not immediately begin ART, repeat testing before initiation of ART is optional if drug-resistance testing was performed at entry into care. In patients with virologic suppression who are switching therapy because of toxicity or for convenience, viral amplification will not be possible; see the Drug-Resistance Testing section for a discussion of the potential limitations and benefits of proviral DNA assays in this situation. Results from prior drug-resistance testing should be considered because they can be helpful in constructing a new regimen.

[h] If a 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 (see the Hepatitis B Virus/HIV Coinfection section).

[i] If HBsAg, HBsAb, and HBcAb test results are negative, HBV vaccine series should be administered. Refer to the HIVMA/IDSA's Primary Care Guidance for Persons with HIV and the Adult and Adolescent Opportunistic Infection Guidelines for detailed recommendations.[1,2]

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

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

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

[m] Serum Na, K, HCO_3, Cl, BUN, creatinine, glucose, and Cr-based eGFR. Serum P should be monitored in patients with CKD who are on TDF-containing regimens.[3]

[n] Consult the HIVMA/IDSA's Clinical Practice Guideline for the Management of Chronic Kidney Disease in Patients Infected with HIV for recommendations on managing patients with renal disease.[3] More frequent monitoring may be indicated for patients with evidence of kidney disease (e.g., proteinuria, decreased glomerular dysfunction) or increased risk of renal insufficiency (e.g., patients with diabetes, hypertension).

[o] CBC with differential should be done when a CD4 count is performed. When CD4 count is no longer being monitored, the recommended frequency of CBC with differential is once a year. More frequent monitoring may be indicated for people receiving medications that potentially cause cytopenia (e.g., TMP-SMX).

[p] If random lipids are abnormal, fasting lipids should be obtained. Consult the American College of Cardiology/American Heart Association's 2018 Guideline on the Management of Blood Cholesterol for diagnosis and management of patients with dyslipidemia.[4]

[q] If random glucose is abnormal, fasting glucose should be obtained. HbA1C is no longer recommended for diagnosis of diabetes in people with HIV on ART (see the American Diabetes Association Guidelines).[5]

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

[s] For persons of childbearing potential.

Key: 3TC = lamivudine; ABC = abacavir; ALT = alanine aminotransferase; ART = antiretroviral therapy; ARV = antiretroviral; AST = aspartate aminotransferase; BUN = blood urea nitrogen; CAB-LA = cabotegravir long-acting; CBC = complete blood count; CD4 = CD4 T lymphocyte; CKD = chronic kidney disease; Cl = chloride; Cr = creatinine; CV = cardiovascular; DAA = direct-acting antiviral; DM = diabetes mellitus; eGFR = estimated glomerular filtration rate; FTC = emtricitabine; HbA1C = hemoglobin A1c; HBcAb = hepatitis B core antibody; HBsAb = hepatitis B surface antibody; HBsAg = hepatitis B surface antigen; HBV = hepatitis B virus; HCO_3 = bicarbonate; HCV = hepatitis C virus; IN = integrase; INSTI = integrase strand transfer inhibitor; K = potassium; Na = sodium; P = phosphorus; PR = protease; PrEP = pre-exposure prophylaxis; RT = reverse transcriptase; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TMP-SMX = trimethoprim-sulfamethoxazole

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[a] (AIII)
After initiating ART	Preferably within 4 to 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 4 to 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 testing every 3 months or more frequently if indicated (AIII).	Every 3 to 6 months (AI)
During the first 2 years of ART	Every 3 months (AIII)	Every 3 months if CD4 <300 cells/mm^3 (BII) Every 6 months if CD4 ≥300 cells/mm^3 (BII)
After 2 years of ART (VL consistently suppressed, CD4 remains <300 cells/mm^3)	Can extend to every 6 months for patients with consistent viral suppression for ≥2 years (AIII).	Every 6 months (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)	Can extend to every 6 months for patients with consistent viral suppression for ≥2 years (AIII).	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 chronic systemic corticosteroids, or antineoplastic therapy)	Every 3 months (AIII)	Perform CD4 count and repeat as clinically indicated[b] (AIII)

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

[b] 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 infection, such as new HIV-associated symptoms, or initiation of treatment with medications that are known to reduce CD4 count.

Key: ART = antiretroviral therapy; CD4 = CD4 T lymphocyte; VL = viral load

Table 5. Recommendations for the Use of Drug-Resistance Assays

Clinical Setting and Recommendation	Rationale
In Early (Acute and Recent) HIV 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 or acquired while using PrEP. The initial ARV 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).
Before ART Initiation in Patients With Chronic HIV Drug-resistance testing is recommended at entry into HIV care to guide the selection of initial ART (AII). A genotypic assay is generally preferred (AIII). Treatment should not be delayed while awaiting results of resistance testing (AIII).	Transmitted HIV with baseline resistance to at least one drug is seen in 9% to 14% of patients, and suboptimal virologic responses may be seen in patients with baseline resistance mutations to ARVs in the prescribed regimen. Some drug-resistance mutations can remain detectable for years in untreated patients with chronic HIV.
If 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). Given the prolonged half-lives of long-acting injectable ARV drugs, INSTI-resistance testing should be considered in all people with HIV who previously received CAB-LA for PrEP, regardless of the time since drug discontinuation (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. INSTI-resistance testing should be ordered for all people with prior exposure to INSTIs for PrEP.
For pregnant people 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 ARV regimen can be modified once resistance test results are available.
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.

Table 5. Recommendations for the Use of Drug-Resistance Assays

Clinical Setting and Recommendation	Rationale
In Patients With Virologic Failure Drug-resistance testing is recommended in patients on combination ART with HIV-RNA levels >200 copies/mL (AI for >1,000 copies/mL, AIII for 501–1,000 copies/mL) and a confirmed HIV RNA 201–500 copies/mL (CIII). In patients with confirmed HIV-RNA levels between 201–500 copies/mL, testing may not be successful but should still be considered.	Drug-resistance testing can help determine the role of resistance in virologic failure and maximize the clinician's ability to select active drugs for the new regimen. Resistance testing for HIV-RNA levels 201–500 copies/mL may need to be conducted within a research setting.
Resistance testing should be done while the patient is taking ART or, if that is not possible, within 4 weeks after discontinuation of non–long-acting ARV drugs (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 ARV regimens and for those with expected 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 ARV 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 in a patient on an INSTI-based regimen or in a patient with a history of INSTI use, 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).
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 ARV regimen and assess the need for a new regimen.
In Pregnant People With HIV Genotypic resistance testing is recommended for all pregnant people 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 people 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 ARV 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.

Table 5. Recommendations for the Use of Drug-Resistance Assays

Clinical Setting and Recommendation	Rationale
In Patients With Undetectable Viral Load or Low-Level Viremia Who Are Planning to Change Their ARV Regimen 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: ART = antiretroviral therapy; ARV = antiretroviral; CAB-LA = cabotegravir long-acting; INSTI = integrase strand transfer inhibitors; NNRTI = non-nucleoside reverse-transcriptase inhibitors; NRTI = nucleoside reverse-transcriptase inhibitors; PI = protease inhibitor; PrEP = pre-exposure prophylaxis

Table 6. Recommended Antiretroviral Regimens for Initial Therapy

Selection of a regimen should be individualized based on virologic efficacy, potential adverse effects, childbearing potential and use of effective contraception, pill burden, dosing frequency, drug–drug interaction potential, comorbid conditions, cost, access, and resistance-test results. A pregnancy test should be performed in persons of childbearing potential, and choice of ART for pregnant individuals should be guided by recommendations from the Perinatal Guidelines. Drug classes and regimens within each class are arranged first by evidence rating and, when ratings are equal, in alphabetical order. See Table 7 for 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. Choice of ART during pregnancy should be guided by recommendations from the Perinatal Guidelines.

For people who do not have a history of CAB-LA use as PrEP, the following regimens are recommended:

INSTI plus Two NRTIs

- BIC/TAF/FTC (AI)[a]
- DTG/ABC/3TC (AI)—if HLA-B*5701 negative
- DTG plus (TAF or TDF)[c] plus (FTC or 3TC) (AI)

INSTI plus One NRTI

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

For people with HIV and a history of CAB-LA use as PrEP, INSTI genotypic resistance testing should be performed before the start of ART. If treatment is begun prior to results of genotypic testing, the following regimen is recommended:

- DRV/c[b] or DRV/r with (TAF or TDF)[c] plus (FTC or 3TC)—pending the results of the genotype test (AIII)

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 fewer 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 Two NRTIs

- EVG/c/(TAF or TDF)[c] FTC (BI)[b]
- RAL plus (TAF or TDF)[c] plus (FTC or 3TC) (BI for TDF/[FTC or 3TC], BII for TAF/FTC)

Boosted PI plus Two NRTIs

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

NNRTI plus Two NRTIs

- DOR/TDF[c]/3TC (BI) or DOR plus TAF[c]/FTC (BIII)

Table 6. Recommended Antiretroviral Regimens for Initial Therapy

- EFV plus (TAF or TDF)[c] plus (FTC or 3TC)
  - EFV 600 mg plus TDF plus (FTC or 3TC) (BI)
  - EFV 400 mg/TDF/3TC (BI)
  - EFV 600 mg plus TAF/FTC (BII)
- RPV/(TAF or TDF)[c]/FTC (BII for TAF and BI for TDF)—if HIV RNA <100,000 copies/mL and CD4 count >200 cells/mm^3

Regimens to Consider When ABC, TAF, and TDF Cannot Be Used or Are Not Optimal

- DTG/3TC (AI), except for individuals with HIV RNA >500,000 copies/mL, HBV coinfection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available
- DRV/r plus RAL twice a day (CI)—if HIV RNA <100,000 copies/mL and CD4 count >200 cells/mm^3
- DRV/r once daily plus 3TC (CI)

Rating of Recommendations: A = Strong; B = Moderate; C = Weak

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

[a] BIC should not be initiated in pregnant people due to insufficient data.

[b] COBI should be avoided in pregnancy because lower concentrations of COBI and its boosted drugs—EVG, DRV, and ATV—have been observed during the second and third trimesters. For individuals with viral suppression who become pregnant while on a COBI-containing regimen and wish to remain on that regimen after counseling regarding lower drug concentration, frequent viral load monitoring is recommended. For further information, refer to the Perinatal Guidelines.

[c] TAF and TDF are two forms of TFV 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.

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

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; CAB-LA = cabotegravir long-acting; 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 = U.S. Food and Drug Administration; FTC = emtricitabine; HBV = hepatitis B virus; HLA = human leukocyte antigen; INSTI = integrase strand transfer inhibitor; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PrEP = pre-exposure prophylaxis; RAL = raltegravir; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TFV = tenofovir

Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios

This table guides clinicians in choosing an initial antiretroviral (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 choice of an initial 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.

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
Pre-ART Characteristics	CD4 count <200 cells/mm^3	Do Not Use the Following Regimens: • RPV-based regimens • DRV/r plus RAL	A higher rate of virologic failure has been observed in those with low pre-treatment CD4 counts.
	HIV RNA >100,000 copies/mL (also see next row if HIV RNA >500,000 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 pre-treatment HIV RNA levels.
	HIV RNA >500,000 copies/mL	Do Not Use the Following Regimens: • RPV-based regimens • ABC/3TC with EFV or ATV/r • DRV/r plus RAL • DTG/3TC	For DTG/3TC, limited data are available in patients with viral loads above this threshold.
	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.
	Prior exposure to CAB-LA PrEP.	Avoid INSTI-based regimens, unless an INSTI genotype shows no resistance mutations. Recommended Regimen Pending INSTI Genotype Results • (DRV/r or DRV/c) plus (TAF or TDF)[a] plus (3TC or FTC)	Mutations conferring resistance to INSTIs have been seen in association with CAB-LA PrEP. CAB-LA has a very long half-life, and drug exposure may persist at levels suboptimal to prevent infection and may select for resistant virus.
	An ARV regimen should be started before HIV drug resistance results are available (e.g., in a person with acute HIV)	Avoid NNRTI-based regimens and DTG/3TC. Avoid ABC.	Transmitted mutations conferring NNRTI and NRTI resistance are more likely than mutations associated with PI or INSTI resistance.

Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
	or when ART is being initiated rapidly.	Recommended ARV Regimens in Persons Without Exposure to CAB-LA PrEP • BIC/TAF/FTC • DTG plus (TAF or TDF)[a] plus (3TC or FTC) • (DRV/r or DRV/c) plus (TAF or TDF)[a] plus (3TC or FTC) Recommended ARV Regimen in Persons on CAB-LA PrEP Prior to HIV Acquisition • (DRV/r or DRV/c) plus (TAF or TDF)[a] plus (3TC or FTC)	HLA-B*5701 results may not be available rapidly, thus ABC is not recommended. Transmitted resistance to DRV, BIC, and DTG is rare, and these drugs have high barriers to resistance. Mutations conferring resistance to INSTIs have been seen in association with CAB-LA PrEP. CAB-LA has a very long half-life, and drug exposure may persist at levels suboptimal to prevent infection and may select for resistant virus.
ART-Specific Characteristics	A one-pill, once-daily regimen is desired.	STR Options as Initial ART Include the Following: • BIC/TAF/FTC • DOR/TDF/3TC • DRV/c/TAF/FTC • DTG/ABC/3TC • DTG/3TC • EFV/TDF/FTC • EFV/TDF/3TC • EVG/c/TAF/FTC • EVG/c/TDF/FTC • RPV/TAF/FTC • RPV/TDF/FTC	Do not use DTG/ABC/3TC if the patient is HLA-B*5701 positive. DTG/3TC is not recommended if HIV RNA is >500,000 copies/mL. Do not use DTG/ABC/3TC or DTG/3TC in the setting of HBV coinfection or unknown HBV status. Do not use RPV-based regimens if HIV RNA is >100,000 copies/mL and CD4 count is <200 cells/mm^3. See Appendix B, Table 12 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.

Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
		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 ≥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)	In general, avoid TDF. ABC may be used if patient is HLA-B*5701 negative. If HIV RNA is >100,000 copies/mL, do not use ABC/3TC plus EFV or ATV/r. TAF may be used if CrCl >30 mL/min or if the patient is on chronic hemodialysis (studied only with EVG/c/TAF/FTC). Consider avoiding ATV. ART Options When ABC, TAF, or TDF Cannot Be Used (For patients with HBV coinfection, consult Hepatitis B Virus/HIV Coinfection for HBV treatment options.) • DTG/3TC (if HIV RNA <500,000 copies/mL) • DRV/r plus 3TC • DRV/r plus RAL (if CD4 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 12 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. Avoid the use of TDF- or TAF-sparing regimens in the setting of HBV coinfection or unknown HBV status, unless also receiving a fully active HBV regimen (see Hepatitis B Virus/HIV Coinfection).
	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 12 for specific dosing recommendations.

Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
			Patients with cirrhosis should be carefully evaluated by an expert in advanced liver disease.
	Concern for excess weight gain	For many people with HIV, gaining weight after starting ART is part of a "return to health." However, some ARV regimens are associated with greater weight gain than others, suggesting that particular drugs may contribute to weight gain.	Initiation of INSTI-containing regimens, particularly BIC and DTG, has been associated with greater weight gain than NNRTI-containing or boosted PI-regimens. Greater weight gain has been observed with initiation of TAF than TDF or with a switch from TDF to TAF. ARV-associated weight gain appears to disproportionately affect women and Black and Hispanic people.
	Osteoporosis	Avoid TDF.[a] ABC may be used if the patient is HLA-B*5701 negative. If HIV RNA is >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[a] 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 preexisting 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 24a, 24b, and 24d) for dosing recommendations when drugs used for psychiatric illnesses are used with certain ARVs.
	HIV-associated dementia	Avoid EFV-based regimens if possible.	The beneficial effects of ART on HIV-associated dementia symptoms may be confounded by EFV-related neuropsychiatric effects.
	Medication-assisted treatment for opioid use disorder	Opioid withdrawal may occur when EFV is initiated in patients who are on a stable dose of methadone. Clinical monitoring is recommended, because medications used to treat	EFV reduces methadone concentrations and may lead to withdrawal symptoms. See the drug–drug interaction tables (Tables 24a, 24b, and 24d) for dosing recommendations.

Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
		opioid dependence may need to be adjusted in some patients.	
	Cardiac QTc interval prolongation	Consider avoiding EFV- or RPV-based regimens if the 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.
	High cardiac risk	Consider avoiding ABC-based regimens. If a boosted PI is the desired option, an ATV-based regimen may have advantages over a DRV-based regimen. Refer to Hyperlipidemia, below, for regimens associated with more favorable lipid profiles.	An increased risk of CV events with ABC has been observed in some studies. Observational cohort studies reported an association between some PIs (DRV and LPV/r) and an increased risk of CV events; this risk has not been seen with ATV (see Protease Inhibitor-Based Regimens). Further study is needed. Certain ARV regimens are associated with more favorable lipid profiles than other regimens, although evidence on whether this improves CV outcomes is lacking.
	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 lowers lipids; therefore, switching from TDF to TAF is associated with increased lipids.	TDF has been associated with lower lipid levels than ABC or TAF.
	Patients with history of poor adherence to non-ARV medications or inconsistent engagement in care	Consider using regimens with a boosted PI or BIC or DTG.	These regimens have a high genetic barrier to resistance.
	Pregnancy	Refer to the Perinatal Guidelines for further guidance on ARV use during pregnancy.	
Presence of Coinfections	HBV infection	Avoid regimens that do not contain NRTIs.	TDF, TAF, FTC, and 3TC are active against both HIV and HBV. 3TC- or FTC-associated HBV mutations can

Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
		Use (TDF or TAF) with (FTC or 3TC) as part of the ARV regimen. If TDF and TAF Are Contraindicated • For treatment of HBV, use FTC or 3TC with entecavir and a suppressive ARV regimen (see Hepatitis B Virus/HIV Coinfection).	emerge rapidly when these drugs are used without another drug that is active against HBV.
	HCV treatment required	Refer to recommendations in Hepatitis C Virus/HIV Coinfection, with special attention to potential interactions between ARV drugs and HCV drugs.	
	Treating TB with rifamycin antibiotics (rifabutin, rifampin, and rifapentine)	Recommended regimens may require dose adjustment. See the drug–drug interaction tables (Table 24a, Table 24b, Table 24c, Table 24d, and Table 24e) and Tuberculosis/HIV Coinfection for information on ARV use with rifamycin antibiotics.	Rifamycin antibiotics are inducers of CYP3A4 and UGT1A1 enzymes, causing significant decreases in concentrations of PIs, INSTIs, and RPV.

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

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; BMD = bone mineral density; CAB-LA = cabotegravir long acting; CD4 = CD4 T lymphocyte; CNS = central nervous system; CrCl = creatinine clearance; CV = cardiovascular; CYP = cytochrome P; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ESRD = end stage renal disease; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FDA = Food and Drug Administration; FPV = fosamprenavir; FTC = emtricitabine; HBV = hepatitis B virus; HCV = hepatitis C virus; HLA = human leukocyte antigen; IDV = indinavir; INSTI = integrase strand transfer inhibitor; LPV/r = lopinavir/ritonavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PI/c = cobicistat-boosted protease inhibitor; PI/r = ritonavir-boosted protease inhibitor; PrEP = pre-exposure prophylaxis; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; STR = single-tablet regimen; TAF = tenofovir alafenamide; TB = tuberculosis; TDF = tenofovir disoproxil fumarate; TFV = tenofovir; UGT = uridine diphosphate glucuronosyltransferase

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

Characteristics	ABC/3TC	3TC[a]	TDF/3TC	TAF/FTC	TDF/FTC
Dosing Frequency	Once daily	Once daily	Once daily	Once daily	Once daily
Available Coformulations for ART-Naive Patients	• ABC/3TC • DTG/ABC/3TC	DTG/3TC	• TDF/3TC • DOR/TDF/3TC • EFV 600 mg/ TDF/3TC • EFV 400 mg/TDF/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
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 cohort studies.	See below	TDF • Renal insufficiency, proximal renal tubulopathy • Decrease in BMD • Renal and bone toxicity are exacerbated by pharmacologic boosters.	TAF • Renal insufficiency, proximal renal tubulopathy (less frequent than with TDF) • Decrease in BMD (less than with TDF; similar to with ABC) • Some studies have reported greater weight gain with TAF than with TDF.	TDF • Renal insufficiency, proximal renal tubulopathy • Decrease in BMD • Renal and bone toxicity are exacerbated by pharmacologic boosters.
	3TC: No significant adverse effects			FTC: Skin discoloration	
Other Considerations	ABC • Perform HLA-B*5701 testing before initiating ABC; if result is positive, do not start ABC and add ABC to patient's allergy list. 3TC • Epivir HBV is for the treatment of HBV and contains a different dose of 3TC than the formulation for ART. Thus, Epivir HBV should not be used for HIV treatment. • Coadministration of 3TC with sorbitol-containing drugs decreases 3TC concentration and should be avoided.			FTC should not be used as sole treatment for HBV due to development of resistance. Discontinuation may precipitate HBV flare if no other agents active against HBV are present.	
	3TC or ABC/3TC should not be used as treatment for HBV due to the development of resistance. Discontinuation may precipitate HBV flare if no other agents active against HBV are present.		• Also used for HBV treatment. Discontinuation may precipitate HBV flare. • See Appendix B, Table 12 for dose recommendations in patients with renal insufficiency.		

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

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

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; BIC = bictegravir; BMD = bone mineral density; CV = cardiovascular; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; 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; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

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

	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 drug resistance mutations	Once daily; requires boosting with COBI	• 400 mg twice daily, *or* • 1,200 mg (two 600-mg tablets) once daily
STR Available for ART-Naive Patients	BIC/TAF/FTC	• DTG/ABC/3TC • DTG/3TC	• EVG/c/TAF/FTC • EVG/c/TDF/FTC	No
Available as an STR	No	Yes	No	Yes, but requires two tablets per dose
Virologic Efficacy Against EVG- or RAL-Resistant HIV	*In vitro* data indicate activity, but clinical trial data are not available.	Yes, for some isolates; effective with DTG 50 mg twice-daily dose	No	No
Adverse Effects	Weight gain, nausea, diarrhea, headache, insomnia; depression and suicidality are rare, occurring primarily in patients with preexisting 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 24d for recommendations regarding dosing separation of INSTIs and these drugs.			
Other Key Potential Drug Interaction Mechanisms	P-gp substrate, 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: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; BIC = bictegravir; COBI = cobicistat; CPK = creatine phosphokinase; CYP = cytochrome P; DTG = dolutegravir; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; INSTI = integrase strand transfer inhibitor; LDL = low density lipoprotein; MATE = multidrug and toxic compound extrusion; OCT2 = organic cation transporter 2; P-gp = p-glycoprotein; 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 (NNRTIs) That Are Recommended as Initial Therapy for People With HIV

Characteristics	DOR	EFV	RPV[a]
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, insomnia, somnolence • Skin rash • QTc prolongation	• Depression, headache • Skin rash • QTc 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.

[a] See Optimizing Antiretroviral Therapy section and Appendix B, Table 4 for information regarding injectable RPV.

Key: 3TC = lamivudine; ART = antiretroviral therapy; CNS = central nervous system; CYP = cytochrome P; DOR = doravirine; EFV = efavirenz; FTC = emtricitabine; H2 = histamine 2; PPI = proton pump inhibitor; QTc = QT corrected for heart rate; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Table 8d. Characteristics of Protease Inhibitor Options That Are Recommended as Initial Therapy for People With HIV

Characteristic	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 generally is recommended. Unboosted ATV also is FDA-approved for ART-naive patients.	DRV only should 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 24a for ATV dosing recommendations when the drug is coadministered with acid-lowering agents.	N/A

Key: ART = antiretroviral therapy; ATV = atazanavir; ATV/c = atazanavir/cobicistat; COBI = cobicistat; CYP = cytochrome P; DRV = darunavir; DRV/c = darunavir/cobicistat; FDA = Food and Drug Administration; FTC = emtricitabine; N/A = not applicable; PI = protease inhibitor; PK = pharmacokinetic; RTV = ritonavir; TAF = tenofovir alafenamide

Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy

Updated: June 3, 2021
Reviewed: June 3, 2021

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 HBV/HIV coinfection • Smaller decline in renal function, less proteinuria, and smaller reductions in BMD than TDF/FTC • Approved for patients with eGFR ≥30 mL/min • Can be used in patients with eGFR <30 mL/min and on chronic hemodialysis	• TDF is associated with lower lipid levels than TAF, perhaps because TDF results in higher plasma levels of tenofovir, which lowers lipids. • See discussion in text regarding weight gain with TAF.
	TDF/3TC	• Coformulated with DOR • Generic formulations are available for TDF, 3TC, TDF/3TC, and 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.

Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
	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.
Single NRTI	3TC	• Coformulated with DTG as STR • Avoids potential toxicities associated with TDF, TAF, ABC	• DTG/3TC is not recommended for individuals with HIV RNA >500,000 copies/mL, HBV coinfection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available.
INSTI	BIC	• Coformulated with TAF/FTC • Higher barrier to resistance than EVG and RAL • No food requirement	• 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 24d. • Inhibits tubular secretion of Cr without affecting glomerular function. • CYP3A4 and UGT1A1 substrate (but not a CYP3A4 inducer or inhibitor); potential for drug–drug interactions. • Should not be used in pregnancy because of lack of data for BIC. • See discussion in text regarding weight gain related to INSTIs.
	DTG	• Higher barrier to resistance than EVG or RAL • Coformulated with ABC/3TC and 3TC • No food requirement • Minimal CYP3A4 interactions • Favorable lipid profile	• 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 24d. • Inhibits renal tubular secretion of Cr and can increase serum Cr without affecting glomerular function.

Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
			• UGT1A1 substrate; potential for drug interactions (see Table 24d). • Depression and suicidal ideation (rare; usually in patients with preexisting psychiatric conditions). • See discussion in text regarding weight gain related to INSTIs. • Updated data from Botswana suggest that DTG exposure during conception may be associated with a small risk of NTDs in the infant compared with non-DTG ARV drugs (1.9 per 1,000 versus 1.1 per 1,000), with a prevalence difference that was not statistically significant. Clinicians should discuss with people of childbearing potential and refer to the Perinatal Guidelines.
	EVG/c	• Coformulated with TDF/FTC or TAF/FTC • Compared with ATV/r, EVG/c causes smaller increases in total and LDL cholesterol. • EVG/c/TAF/FTC can be used in patients on chronic hemodialysis.	• EVG/c/TDF/FTC is recommended only 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 24d. • 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 preexisting psychiatric conditions). • EVG/c should be avoided in pregnancy, because levels of COBI and its boosted drugs are lower in the second and third trimesters. If women who are pregnant with suppressed virus on EVG/c elect to continue on the drug, frequent viral load monitoring is recommended. • See discussion in text regarding weight gain related to INSTIs.

Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
	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 FDC formulation. • Oral absorption of RAL can be reduced by simultaneous administration with drugs containing polyvalent cations (e.g., Al-, Ca-, or Mg-containing antacids or supplements or multivitamin tablets with minerals). See dosing recommendations in Table 24d. • UGT1A1 substrate; potential for drug interactions (see Table 24d). • Depression and suicidal ideation (rare; usually in patients with preexisting psychiatric conditions). • See discussion in text regarding weight gain related to INSTIs.
NNRTI	DOR	• Coformulated with TDF/3TC • Compared to EFV, fewer CNS side effects • No food requirement • Favorable lipid profile • Lack of association with weight gain compared with boosted DRV or EFV	• Shorter-term clinical experience than with EFV and RPV. • Potential for CYP450 drug interactions (see Tables 24b, 25a and 25b). • 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. Late-onset ataxia and encephalopathy also have been reported. • Periodic screening for depression and suicidality is recommended in people with HIV who are taking a regimen that includes EFV. • Dyslipidemia • Rash

Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
		• EFV 400 mg has fewer CNS side effects than EFV 600 mg. • EFV 600 mg can be given with rifamycin antibiotics (rifampin, rifabutin, or rifapentine).	• 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 24b and 25a). • Should be taken on an empty stomach (food increases drug absorption and CNS toxicities).
	RPV	• Coformulated with TDF/FTC and TAF/FTC • RPV/TDF/FTC and RPV/TAF/FTC have smaller pill sizes than other coformulated ARV drugs • Compared with EFV: o Fewer CNS adverse effects o Fewer lipid effects o Fewer rashes	• Not recommended in patients with pre-ART HIV RNA >100,000 copies/mL or CD4 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 24b and 25a). • Meal requirement (>390 kcal) • Requires acid for adequate absorption. o Contraindicated with PPIs. o Use with H2 antagonists or antacids with caution (see Table 24a for detailed dosing information).

Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
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 are available as generics.	• Commonly causes indirect hyperbilirubinemia, which may manifest as scleral icterus or jaundice. • Food requirement • Absorption depends on food and low gastric pH (see Table 24a for interactions with H2 antagonists, antacids, and PPIs). • Nephrolithiasis, cholelithiasis, nephrotoxicity • GI adverse effects • CYP3A4 inhibitors and substrates: potential for drug interactions (see Table 24a).
	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. • COBI should be avoided in pregnancy, because levels of COBI and its boosted drugs are lower in the second and third trimesters. If women who are pregnant with suppressed virus on ATV/c elect to continue on the drug, frequent viral load monitoring is recommended.
	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 24a). • Increased CV risk reported in one observational cohort study. • Hepatotoxicity has been reported, especially in those with preexisting liver disease.

Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
	DRV/c Specific considerations	• Coformulated as DRV/c and DRV/c/TAF/FTC.	• COBI inhibits active tubular secretion of Cr and can increase serum Cr without affecting renal glomerular function. • Coadministration with TDF is not recommended in patients with CrCl <70 mL/min. • COBI (like RTV) is a potent CYP3A4 inhibitor, which can result in significant interactions with CYP3A substrates. • COBI should be avoided in pregnancy, because levels of COBI and its boosted drugs are lower in the second and third trimesters. If women who are pregnant with suppressed virus on DRV/c elect to continue on the drug, frequent viral load monitoring is recommended.

Key: 3TC = lamivudine; ABC = abacavir; Al = aluminum; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; BMD = bone mineral density; Ca = calcium; CD4 = CD4 T lymphocyte; CNS = central nervous system; COBI = cobicistat; Cr = creatinine; CrCl = creatinine clearance; CV = cardiovascular; CYP = cytochrome P; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; eGFR = estimated glomerular filtration rate; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FDC = fixed-dose combination; FPV = fosamprenavir; FTC = emtricitabine; GI = gastrointestinal; HBV = hepatitis B virus; HLA = human leukocyte antigen; HSR = hypersensitivity reaction; IDV = indinavir; INSTI = integrase strand transfer inhibitor; LDL = low-density lipoprotein; LPV/r = lopinavir/ritonavir; Mg = magnesium; 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

ARV Components or Regimens	Reasons for *Not* Recommending as Initial Therapy
Combination INSTI plus NNRTI	
CAB plus RPV (PO or IM)	• This regimen only is approved for people who have achieved viral suppression on another ARV regimen. It has not been studied as initial ARV regimen.
DTG plus RPV	• This regimen only is approved for people who have achieved viral suppression on another ARV regimen. It has not been studied as initial ARV regimen.
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
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

Table 10. Antiretroviral Components or Regimens Not Recommended as Initial Therapy

ARV Components or Regimens	Reasons for *Not* Recommending as Initial Therapy
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	
FTR gp120 Attachment Inhibitor	• Only studied in a very small number of patients with virologic failure
IBA CD4 Post-Attachment Inhibitor	• Only studied in a very small number of patients with virologic failure • Requires IV therapy

Table 10. Antiretroviral Components or Regimens Not Recommended as Initial Therapy

ARV Components or Regimens	Reasons for *Not* Recommending as Initial Therapy
	• High cost
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
T20 Fusion Inhibitor	• Only studied in patients with virologic failure • Twice-daily subcutaneous injections • High rate of injection site reactions

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; CAB = cabotegravir; CD4 = CD4 T lymphocyte; COBI = cobicistat; d4T = stavudine; ddI = didanosine; DLV = delavirdine; DRV = darunavir; DTG = dolutegravir; ECG = electrocardiogram; EFV = efavirenz; ETR = etravirine; FPV = fosamprenavir; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; FTR = fostemsavir; GI = gastrointestinal; IBA = ibalizumab; IDV = indinavir; IDV/r = indinavir/ritonavir; IM = intramuscular; 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 = oral; RPV = rilpivirine; RTV = ritonavir; SJS = Stevens Johnson Syndrome; SQV = saquinavir; SQV/r = saquinavir/ritonavir; T20 = enfuvirtide; TDF = tenofovir disoproxil fumarate; TEN = toxic epidermal necrolysis; TPV = tipranavir; TPV/r = tipranavir/ritonavir; ZDV = zidovudine

Table 11. Antiretroviral Options for Patients with Virologic Failure

Designing a new regimen for patients who are experiencing treatment failure should always be guided by ARV history and results from current and past resistance testing. This table summarizes the text above and displays the most common or likely clinical scenarios seen in patients with virologic failure. For more detailed descriptions, please refer to the texts above and/or consult an expert in HIV 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.

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

Table 11. Antiretroviral Options for Patients with Virologic Failure

Clinical Scenario	Type of Failing Regimen	Resistance Considerations	New Regimen Options[a,b]	Goal
		If failure on EVG or RAL, often have INSTI resistance, but potentially susceptible to DTG Can have 3TC or FTC resistance	Boosted PI plus two NRTIs (preferably at least one fully active*) (AIII); *or* DTG[e] twice daily or possibly BIC (if HIV is sensitive) plus two fully active NRTIs (BIII); *or* DTG[e] twice daily or possibly BIC (if HIV is sensitive) plus a boosted PI (AIII)	Resuppression
Second Regimen Failure and Beyond	Drug resistance with fully active treatment options—	Use past and current genotypic- +/– phenotypic-resistance testing and ART history when designing new regimen.	New regimen according to original treatment type—	Resuppression
	(i) Boosted PI, but not second-generation INSTI, fully active		(i) Boosted PI with two NRTIs (preferably at least one fully active)	
	(ii) Second-generation INSTI, but not boosted PI, fully active		(ii) DTG or BIC with two NRTIs (preferably at least one fully active)	
	(iii) Both PI and INSTI fully active		(iii) The two options above or boosted PI with INSTI	
	Multiple or extensive drug resistance with few treatment options (e.g., fully active boosted PI or second-generation INSTI unavailable)	Use past and current genotypic- and phenotypic-resistance testing to guide therapy. Confirm with a viral tropism assay when use of MVC is considered. Consult an expert in drug resistance if needed.	New regimen should include at least two, and preferably three, fully active agents, including those with novel mechanisms of action (e.g., IBA, FTR, LEN). If <3 fully active drugs, include as many fully active drugs as possible, along with potentially partially active drugs. Consider enrollment into clinical trials or expanded access programs for investigational agents if available. Discontinuation of all ARV drugs is not recommended.	Resuppression if possible; otherwise, keep viral load as low as possible and CD4 count as high as possible.

Table 11. Antiretroviral Options for Patients with Virologic Failure

ART-Experienced Patients with Suspected Drug Resistance and Limited or Incomplete ARV 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 with careful monitoring of virologic response and early resistance testing if inadequate virologic suppression. If no ARV history is available, consider initiating a regimen with drugs with high genetic barriers to resistance (e.g., DTG, BIC, and/or boosted DRV) with careful monitoring of virologic response and early resistance testing, if inadequate virologic suppression.	Resuppression

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

[b] When switching an ARV regimen in a patient with HBV/HIV coinfection, ARV drugs that are active against HBV and have high resistance barrier to 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] CI for LPV/r + RAL; AIII for other boosted PIs (e.g., DRV) or INSTIs (e.g., DTG).

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

* See text for details and additional options in special settings.

Key: 3TC = lamivudine; ART = antiretroviral therapy; ARV = antiretroviral; BIC = bictegravir; CD4 = CD4 T lymphocyte; DRV = darunavir; DTG = dolutegravir; EVG = elvitegravir; FTC = emtricitabine; FTR = fostemsavir; HBV = hepatitis B virus; IBA = ibalizumab; INSTI = integrase strand transfer inhibitor; LEN = lenacapavir; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; RAL = raltegravir

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

Suspicion of Acute HIV Infection

- Health care providers should consider the possibility of acute HIV infection in individuals with the signs, symptoms, or laboratory findings described below and in asymptomatic individuals with a possible recent (within 2–6 weeks) exposure to HIV.[a]
  - Signs, symptoms, or laboratory findings of acute HIV infection may include, but are not limited to, one or more of the following: fever, lymphadenopathy, skin rash, myalgia, arthralgia, headache, diarrhea, pharyngitis, oral ulcers, leucopenia, thrombocytopenia, and transaminase elevation.
  - High-risk exposures include sexual contact with a person who has HIV or a person at risk of HIV infection; sharing needles and syringes to inject drugs, as well as equipment used to prepare drugs for injection; or any exposure in which an individual's mucous membranes or any breaks in the skin come in contact with bodily fluid that potentially carries HIV.

Differential Diagnosis

- The differential diagnosis of acute HIV infection may include, but is not limited to, viral illnesses, such as COVID-19, EBV and non-EBV (e.g., CMV) infectious mononucleosis syndromes, influenza, viral hepatitis, streptococcal infection, or syphilis. Diagnosis of any STI should prompt HIV testing and consideration of acute HIV infection.

Testing to Diagnose/Confirm Acute HIV Infection

- Acute HIV infection is defined as detectable HIV RNA or p24 antigen (the specific antigen used in currently available HIV-1/2 Ag/Ab combination assays) in the setting of a negative or indeterminate HIV antibody test result.
- A reactive HIV antibody test result or Ag/Ab combination test result must be followed by supplemental confirmatory testing.
- A negative or indeterminate HIV antibody test result in a person with a reactive Ag/Ab test result or in whom acute HIV infection is suspected requires plasma HIV RNA testing to diagnose acute HIV infection.
- A positive result on a quantitative or qualitative plasma HIV RNA test in the setting of a negative or indeterminate antibody test result indicates that acute HIV infection is highly likely. In this case, the diagnosis of HIV infection should be confirmed by subsequent documentation of HIV antibody seroconversion.
- A positive HIV Ag/Ab test result or a positive HIV RNA test result in the setting of a negative HIV antibody test result in a person taking PrEP should prompt immediate confirmation of HIV diagnosis. It is important to collect a new blood specimen to verify the HIV diagnosis before initiating HIV treatment.

Antiretroviral Therapy After Diagnosis of Early HIV Infection

- ART is recommended for all people with HIV, including those with early HIV infection (AI). ART should be initiated as soon as possible after HIV diagnosis (AII).
- Once initiated, the goals of ART are to achieve sustained plasma virologic suppression and to prevent HIV transmission (AII).
- All persons of childbearing potential who receive a diagnosis of early HIV infection should have a pregnancy test (AIII).
- Pregnant people with early HIV infection should begin ART as soon as possible for their own health and to prevent perinatal transmission of HIV (AI).
- A blood sample for genotypic drug-resistance testing should be obtained before initiating ART to guide the selection of the regimen (AIII), but ART should be initiated as soon as possible, often before resistance-test results are available. If resistance is subsequently identified, treatment should be modified as needed.
- ART can be initiated before the results of drug-resistance testing are known. For individuals who do not have a history of using CAB-LA as PrEP, one of the following ARV regimens is recommended (AIII):
  - DTG with (TAF or TDF)[b] plus (FTC or 3TC)
  - BIC/TAF/FTC

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

- Boosted DRV with (TAF or TDF)[b] plus (FTC or 3TC)

- For individuals with a history of using CAB-LA as PrEP, genotypic resistance testing done before starting ART should include screening for INSTI-resistance mutations (AIII). Recommended regimens include the following:
  - Boosted DRV with (TAF or TDF)[b] plus (FTC or 3TC)—pending the results of the genotype (AIII). Empiric INSTI-containing regimens are not recommended (AIII), because INSTI resistance may be present in those who become infected during the use of CAB-LA and possibly up to 4 years after.
- Pregnancy testing should be performed in people of childbearing potential before initiating ART (AIII).

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

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

Key: 3TC = lamivudine; Ag/Ab = antigen/antibody; ART = antiretroviral therapy; ARV = antiretroviral; BIC = bictegravir; CAB-LA = cabotegravir long-acting; CMV = cytomegalovirus; DRV = darunavir; DTG = dolutegravir; EBV = Epstein-Barr virus; FTC = emtricitabine; INSTI = integrase strand transfer inhibitor; PrEP = pre-exposure prophylaxis; STI = sexually transmitted infection; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Table 13. Antiretroviral Therapy-Specific Strategies to Improve Medication Adherence

Antiretroviral Therapy-Specific Strategies to Improve Medication Adherence	
Regimen selection	• Simple ART regimens (e.g., fixed-dose, once daily combinations) with high barriers to resistance are preferable, if possible.[35] • Minimal side effects (e.g., gastrointestinal)
Treatment plan	• Develop the plan in partnership with AYA with HIV, considering daily schedule; tolerance of pill number, size, and frequency; issues affecting absorption; and potential adverse effects and interactions with other medications.[34,36] • Design adolescent-friendly reminder systems[37] (e.g., apps, cell phone reminders, pill boxes) for adherence support.[38]
Motivators	• Emphasize personal benefits (e.g., viral suppression, improved health). • Undetectable equals untransmittable (U=U) status disclosure to sexual partners without HIV may act as a particularly strong motivator for reducing stigma and improving adherence among AYA with HIV.

Table 14: Approaches to Optimize Care Transition for AYA With HIV

Pediatric/Adolescent	Adult
Personnel	
• Engage a multidisciplinary team knowledgeable about medical and psychosocial issues of AYA with HIV, including the challenges of transitioning youth to adult care settings. • Utilize combined internal medicine and pediatrics-trained providers if available. • Assign a transition point person and have their contact information readily available. • Educate HIV care teams and staff about transitioning AYA with HIV and their needs.	• Engage a multidisciplinary adult care team knowledgeable about medical and psychosocial issues of AYA with HIV, including the challenges of transitioning youth to adult care settings. • Utilize combined internal medicine and pediatrics providers if available. • Assign a transition point person and have their contact information readily available. • Identify outreach specialists, navigators, social workers, case managers, and providers with a youth-friendly approach. • Educate clinic personnel about AYA with HIV and their challenges to enhance sensitivity and understanding and minimize stigma.
Education and Preparation of AYA with HIV	
• Enhance AYA with HIV health literacy, including understanding of HIV and their medical history. • Address patient and family resistance to transition of care caused by lack of information, concerns about stigma or risk of disclosure, and differences in practice styles. • Help youth develop life skills, including, but not limited to, counseling on appropriate use of a primary care provider and how to manage appointments; the importance of prompt symptom recognition and reporting; and self-efficacy in managing medications, insurance, and assistance benefits.	• Meet AYA with HIV before transition, if possible. • Clearly outline policies and expectations before and during the first visit. • Have an orientation plan to acquaint newly transitioned AYA with HIV to the clinic environment and adult clinical care program. • Implement interventions that may improve outcomes, such as patient navigators, peer support groups, mental health assessment, and inclusion of parents and guardians where available. • Address health literacy and ensure AYA with HIV understand HIV, goals of care, etc. • Continue to work with AYA with HIV toward developing life skills, etc.
Strategies and Approaches	
• Identify adult care providers able to provide youth-friendly care for adolescents and young adults. • Develop a formal, purposeful individualized transition plan to address comprehensive care needs, including medical, psychosocial, and financial aspects of transitioning to adult HIV care. • Optimize provider communication between adolescent and adult clinics, including a warm multidisciplinary, comprehensive medical history hand-off that includes prior regimens and outcomes (e.g., adherence, virologic failure and resistance).	• Develop a realistic clinic model based on specific needs (e.g., simultaneous transition of mental health and/or case management versus a gradual phase-in) and staffing. • Engage in a warm handoff from the pediatric team, which allows the accepting adult team to learn about and understand the multidisciplinary challenges and goals for the patient. Devise a plan for how to continue building the skills on the adult side. • Build in flexibility (e.g., permissive grace period for appointments, leniency for missed appointments, particularly when first transitioning). • Incorporate other aspects of care beyond HIV management, if possible (e.g., family planning, sexually transmitted infection testing and treatment, mental health, substance use).

Table 14: Approaches to Optimize Care Transition for AYA With HIV

Pediatric/Adolescent	Adult
Communication	
• Foster regular dialogue between pediatric and adolescent and adult teams before and after transition through regular meetings, case conferences, etc. • Solicit feedback from the AYA with HIV • Use technology (e.g., texting, HIPAA-compliant messaging apps, telemedicine).	
Evaluation	
• Implement ongoing evaluation to measure the success of the selected model (retention in adult care).	

Table 15: AYA With HIV ARV Adherence Barriers and Strategies to Support Adherence

ART Adherence Barrier	Adherence Support Strategy	Rationale for Adherence Support Strategy
Prioritization of short-term goals and socialization with peers over daily HIV treatment adherence	Youth-friendly reminder systems (e.g., text, phone, apps)	• Daily adherence to ARV regimens may not take priority in the lives of AYA with HIV. • AYA with HIV benefit from reminder systems to facilitate adherence.
	Novel ART delivery strategies (e.g., long-acting oral or injectable ARVs)	• AYA with HIV show interest in long-acting alternatives for ART delivery. • Long-acting ARVs are a promising tool to facilitate adherence, once approved for AYA with HIV.
Social concerns related to loss of confidentiality	Simple ARV regimens	• Adolescents do not want to be different from peers; adherence to complex regimens is particularly challenging. • Simple ARV regimens are preferable for AYA with HIV.
	User-friendly and discreet regimens	• Avoidance of HIV-related stigma and of unintentional disclosure of HIV status is a priority for AYA with HIV. • Protect confidentiality with user-friendly and discreet adherence supports (e.g., discreet pill bottles, reminder systems, etc.).
Side effects/fear of side effects	ARV regimens that minimize side effects	• Side effects are associated with nonadherence to ARVs. • Regimens with minimal side effects and medications that manage side effects have utility for AYA with HIV.
Denial or dismissal of HIV diagnosis	Motivational interviewing (MI) and motivational enhancement therapy (MET)	• MI and MET acknowledge AYA with HIV's autonomy and potential ambivalence about treatment adherence. • MI and MET have shown promise for improving adherence to chronic disease treatment, including HIV.
	Positive affirmation messages (e.g., text, app)	• Electronically delivered positive affirmation messages can improve self-esteem and ARV adherence among AYA with HIV.
Lack of health literacy regarding the benefits of ART	Health literacy support and U=U education	• AYA with HIV may not fully understand the importance of taking ARVs daily, particularly when they are asymptomatic. • Increased health literacy is associated with better adherence to ARV regimens. • U=U education holds promise for AYA with HIV.
Mistrust of providers and the medical establishment	Empathetic and patient-centered communication	• Communication exploring the needs of AYA with HIV patients can build trust, including exploring needs not directly related to HIV treatment (e.g., school, employment, relationships, etc.).
Mental health and/or substance use	Individualized mental health and substance use services	• Comprehensive mental health and substance use services have shown promise for improving viral suppression among AYA with HIV. • Service should be delivered based on individualized needs assessments.

Table 15: AYA With HIV ARV Adherence Barriers and Strategies to Support Adherence

ART Adherence Barrier	Adherence Support Strategy	Rationale for Adherence Support Strategy
	Directly observed therapy may be considered	• For some AYA with HIV with difficult adherence problems, directly observed therapy may be considered.
Lack of familial and social support	Family and peer support groups	• Family members and peers are a defense against stigma and social isolation, source of emotional support, and partners in medication management. • Family and peer support groups have utility for AYA with HIV living with HIV.
Provider views of AYA with HIV as "risky" and/or not ready for ART	Promote development of a positive rather than risk-centered identity among AYA with HIV	• Adolescence and young adulthood are periods of identity development where HIV stigma is particularly problematic. • Providers should not conceptualize AYA with HIV as "high risk" to reduce stigma and improve ARV adherence.
Provider implicit biases of AYA with HIV	Implicit bias training	• Consciously changing biased associations and repeated bias self-regulation training can reduce providers' implicit biases.
	Gender-affirming care	• Transgender individuals are more likely to achieve viral suppression when HIV care providers affirm their gender (e.g., use chosen name and pronoun). • For a more detailed discussion, see guidelines for Transgender People with HIV.

Table 15: AYA With HIV ARV Adherence Barriers and Strategies to Support Adherence

ART Adherence Barrier	Adherence Support Strategy	Rationale for Adherence Support Strategy
Lack of youth-friendly services	Dedicated youth HIV clinic	• Clinic days or hours dedicated to AYA with HIV patients better address unique adherence needs; youth-friendly services include the following: o flexible hours, easy scheduling, telephone/telehealth appointments; o providers trained in working with AYA with HIV; o youth-friendly waiting rooms and physical spaces; o supplemental services that comprehensively address psychosocial and health needs of AYA with HIV; and o incentives for AYA with HIV care engagement.
	Youth-friendly hours, staff, and physical space	• Where dedicated hours and services are not possible, youth-friendly service elements can be integrated into existing clinic structures, e.g.: o offering evening hours; o staff training on service delivery to AYA with HIV; and o youth-friendly waiting rooms and physical spaces.
	Referrals to more youth-friendly HIV providers	• Where youth-friendly services are not possible, referrals to more youth-friendly HIV care providers should be considered. • Referral decisions should be made collaboratively with the patient.
Lack of comprehensive services that address common psychosocial stressors	Supplemental health, behavioral health, and psychosocial support services	• Individualized delivery of comprehensive supplemental services helps address unique needs of AYA with HIV, including the following: o primary care and sexual and reproductive health services; o behavioral health services; and o psychosocial support services (e.g., school support, transportation, support groups, housing and food assistance).
	Collaboration with and referrals to outside support services	• Where delivery of comprehensive supplemental services is not possible, collaborations with and referrals to outside support services should be considered.

Key: ART = antiretroviral treatment; ARV = antiretroviral; AYA = adolescent and young adult; U=U = undetectable equals untransmittable

Table 16. 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, because improper administration will result in poor absorption and low drug levels.
Methadone	Individualize the 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 be prescribed for OUD only 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 with placebo after transition from prison to community.
Nicotine Use Disorder			
Nicotine Replacement Therapy	FDA has approved a wide variety of 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 3 days, then increase to either 150 mg twice daily or 300 mg once daily (use only 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 ideally should be 1 week after starting therapy.

Table 16. Medications for Treatment of Substance Use Disorders

Medication	Dose and Recommendations	Potential Interaction with ARV Drugs	Comments
Varenicline	Titrate the dose based on tolerability until the 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 ideally should 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

Table 17. 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 24a, 24b, 24c, 24d, and 24e 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 18. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of Hepatitis C Virus in Adults With HIV

The recommendations in this table for concomitant use of select HIV drugs with U.S. Food and Drug Administration (FDA)–approved HCV DAA drugs are based on available pharmacokinetic (PK) interaction data or are predictions based on the known metabolic pathways of the agents. (Instances where PK interaction data are limited or not available are indicated in the table.) Whenever HIV and HCV drugs are used concomitantly, patients should be closely monitored for HIV and HCV virologic efficacy and potential toxicities. Because the field of HCV therapy is rapidly evolving, readers also should refer to the latest drug product labels and the HCV Guidance for updated information.

Note: Interactions with fosamprenavir (FPV) and nelfinavir (NFV) are **not** included in this table. Please refer to the FDA product labels for information regarding drug interactions with these HIV protease inhibitors (PIs).

ARV Drugs	Individual Drug	Coformulated				
				SHOULD NOT BE USED IN THOSE WITH MODERATE TO SEVERE HEPATIC IMPAIRMENT (Cirrhosis classified as Child-Pugh class B or C)		
	Sofosbuvir	Ledipasvir/ Sofosbuvir	Sofosbuvir/ Velpatasvir	Sofosbuvir/ Velpatasvir/ Voxilaprevir	Glecaprevir/ Pibrentasvir	Elbasvir/ Grazoprevir
3TC	✓	✓	✓	✓	✓	✓
ABC	✓	✓	✓	✓	✓	✓
FTC	✓	✓	✓	✓	✓	✓
TAF	✓	✓	✓	✓	✓	✓
TDF	✓	✓ Monitor for TDF-associated adverse events.	✓ Monitor for TDF-associated adverse events.	✓ Monitor for TDF-associated adverse events.	✓	✓
Unboosted ATV	✓	✓	✓	✖	✖	✖
ATV/r or ATV/c	✓	✓	✓	✖	✖	✖

Table 18. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of Hepatitis C Virus in Adults With HIV

ARV Drugs	Individual Drug	Coformulated				
				SHOULD NOT BE USED IN THOSE WITH MODERATE TO SEVERE HEPATIC IMPAIRMENT (Cirrhosis classified as Child-Pugh class B or C)		
	Sofosbuvir	Ledipasvir/ Sofosbuvir	Sofosbuvir/ Velpatasvir	Sofosbuvir/ Velpatasvir/ Voxilaprevir	Glecaprevir/ Pibrentasvir	Elbasvir/ Grazoprevir
DRV/r or DRV/c	✓	If a PI/r or PI/c is used with TDF, ↑ TDF concentrations are expected. If coadministration is necessary, monitor for TDF-associated adverse events.[a]	If a PI/r or PI/c is used with TDF, ↑ TDF concentrations are expected. If coadministration is necessary, monitor for TDF-associated adverse events.[a]	✓ If a PI/r is used with TDF, ↑ TDF concentrations are expected. Monitor for TDF-associated adverse events.[a] Consider monitoring for hepatotoxicity.[b]	✗	✗
LPV/r	✓			✗	✗	✗
TPV/r	✗	✗	✗	✗	✗	✗
DOR	✓	✓ If used with TDF, monitor for TDF-associated adverse events.	✓	✓	✓	✓
EFV	✓		✗	✗	✗	✗
ETR	✓		✗	✗	✗	✗
NVP	✓		✗	✗	✗	✗
RPV PO and IM	✓		✓	✓	✓	✓
BIC/TAF/FTC	✓	✓	✓	✓	✓	✓
CAB PO and IM	✓	✓	✓	✓	✓	✓
DTG	✓	✓ If used with TDF, monitor for TDF-associated adverse events.	✓	✓	✓	✓

Table 18. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of Hepatitis C Virus in Adults With HIV

ARV Drugs	Individual Drug	Coformulated				
				SHOULD NOT BE USED IN THOSE WITH MODERATE TO SEVERE HEPATIC IMPAIRMENT (Cirrhosis classified as Child-Pugh class B or C)		
	Sofosbuvir	Ledipasvir/ Sofosbuvir	Sofosbuvir/ Velpatasvir	Sofosbuvir/ Velpatasvir/ Voxilaprevir	Glecaprevir/ Pibrentasvir	Elbasvir/ Grazoprevir
EVG/c/TDF/FTC	✓	✖	✓ If used with TDF, monitor for TDF-associated adverse events.	✓ If used with TDF, monitor for TDF-associated adverse events. Consider monitoring for hepatotoxicity.[b]	✓ If used with TDF, monitor for TDF-associated adverse events. Consider monitoring for hepatotoxicity.[c]	✖
EVG/c/TAF/FTC	✓	✓	✓	✓ Consider monitoring for hepatotoxicity.[e]	✓ Consider monitoring for hepatotoxicity.[f]	✖
RAL	✓	✓	✓	✓	✓	✓
MVC	✓	✓	✓	✓	✓	✓
FTR	✓	✓	✓	✖ Use alternative HCV regimen if possible.	✓	✖ Use alternative HCV regimen if possible.
LEN	✓	✓	✓	✓	✓	✓

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

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

[c] Glecaprevir exposures can increase when it is coadministered with EVG/c. Until more safety data in clinical settings become 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

Table 18. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of Hepatitis C Virus in Adults With HIV

? = Data on PK interactions with ARV drug are limited or not available
↑ = Increase
↓ = Decrease

Key: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; CAB = cabotegravir; DAA = direct-acting antiviral; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; FTR = fostemsavir; HCV = hepatitis C virus; IM = intramuscular; LEN = lenacapavir; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NVP = nevirapine; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; PK = pharmacokinetic; PO = oral; RAL = raltegravir; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV/r = tipranavir/ritonavir

Table 19. Strategies to Improve Linkage to Care, Retention in Care, Adherence to Appointments, and Adherence to Antiretroviral Therapy

Strategies	Examples
Provide an accessible, trustworthy, nonjudgmental multidisciplinary health care team.	• Include care providers, nurses, social workers, case managers, pharmacists, medication managers, and administrative staff on the care team; train all members on providing compassionate and patient-centered care.
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). • Actively support linkage to care with assistance in making appointments and linkage to services to overcome barriers to care. • Streamline Ryan White HIV/AIDS Program eligibility verification processes for uninsured and underinsured clients.
Evaluate the 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 when starting ART and on an ongoing basis.	• Assess the patient's cognitive competence and impairment. • Assess behavioral and psychosocial challenges, including depression, mental illnesses, trauma, 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, and transportation problems.
Provide needed resources.	• Provide or refer for mental health and/or substance use treatment. • Provide resources to obtain prescription drug coverage (e.g., AIDS Drug Assistance Programs (ADAPs), Pharmaceutical Company HIV Patient Assistance Programs and Cost-Sharing Assistance Programs). • Assist patients during insurance enrollment periods to facilitate enrollment in plans that cover antiretrovirals. • Provide resources about stable housing, social support, transportation assistance, and income and food security.

Table 19. Strategies to Improve Linkage to Care, Retention in Care, Adherence to Appointments, and Adherence to Antiretroviral Therapy

Strategies	Examples
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 or BIC-based ART if poor adherence is anticipated. • Consider use of STR or fixed-dose-combination formulations to reduce pill burden. • Consider use of long-acting injectables in people with suppressed viral load if clinically appropriate. • Assess if the cost or 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 benefits of low or nondetectable levels of HIV viral load (e.g., "Undetectable = Untransmittable") and increases in CD4 cell counts. • Thank patients for attending their appointments.
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. • The patient is unaware of appointments, or appointments are not scheduled with proper patient input. • Cost-related issues (e.g., copays for medications or visits, missed work time). • Depression, drug and alcohol use, homelessness, or poverty. • Stigma of taking pills or attending HIV-related appointments. • Nondisclosure of status or privacy concerns leading to missed doses, refills, or appointments.

Table 19. Strategies to Improve Linkage to Care, Retention in Care, Adherence to Appointments, and Adherence to Antiretroviral Therapy

Strategies	Examples
Select from among available effective adherence and retention interventions.	• See the CDC's Compendium of Evidence-Based Interventions and Best Practices for HIV Prevention 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, pharmacy delivery). • Use patient prescription assistance programs (see above in the table, 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 for persons in substance use treatment (if feasible). • Enhance clinic support and structures to promote linkage and retention (e.g., reminder calls, flexible scheduling, open access, active referrals, improved patient satisfaction). • Offer telehealth services for primary care, as well as supportive services when appropriate.
Systematically monitor retention in care.	• Record and follow up on missed visits.

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

Table 20. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy

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

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

In this table, N/A indicates either that there are no reported cases for that particular side effect or that data for that specific ARV drug class are not available. See Appendix B, Tables 3, 4, 5, 6, 7, 8, 9, and 10 for additional information listed by drug.

Adverse Effect	Drug Class					
	NRTIs	NNRTIs	PIs	INSTIs	EIs	CI
Bone Density Effects	TDF: Associated with greater loss of BMD than other NRTIs, especially when given with a PK booster. 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	Not evaluated
Bone Marrow Suppression	ZDV: Anemia, neutropenia.	N/A	N/A	N/A	N/A	N/A
Cardiac Conduction Effects	N/A	RPV and EFV: QTc prolongation	ATV/r and LPV/r: PR prolongation. Risk factors include pre-existing heart disease and concomitant use of	N/A	FTR: QTc prolongation was seen at four times the recommended dose. Use with caution in patients with pre-existing heart disease or QTc prolongation, or concomitant use	N/A

Table 20. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy

Adverse Effect	Drug Class					
	NRTIs	NNRTIs	PIs	INSTIs	EIs	CI
			medications that may cause PR prolongation.		of medications that may prolong QTc interval.	
Cardiovascular Disease	ABC: Associated with an increased risk of MI in some cohort studies. Absolute risk greatest in patients with traditional CVD risk factors.	N/A	Boosted DRV and LPV/r: Associated with cardiovascular events in some cohorts	N/A	N/A	N/A
Cholelithiasis	N/A	N/A	ATV: Cholelithiasis and kidney stones may present concurrently. Median onset is 42 months after ARV initiation.	N/A	N/A	N/A
Diabetes Mellitus and Insulin Resistance	ZDV	N/A	LPV/r, but not with boosted ATV or DRV	N/A	N/A	N/A
Dyslipidemia	ZDV > ABC: ↑ TG and ↑ LDL TAF: ↑ TG, ↑ LDL, and ↑ 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 > DRV/r and ATV/r: ↑ TG	EVG/c: ↑ TG, ↑ LDL, ↑ HDL	N/A	N/A
Gastrointestinal Effects	ZDV > other NRTIs: Nausea and vomiting	N/A	GI intolerance (e.g., diarrhea, nausea, vomiting) LPV/r > DRV/r and ATV/r: Diarrhea	EVG/c: Nausea and diarrhea	N/A	LEN: Nausea and diarrhea

Table 20. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy

Adverse Effect	Drug Class					
	NRTIs	NNRTIs	PIs	INSTIs	EIs	CI
Hepatic Effects	When TAF, TDF, 3TC, and FTC are withdrawn in patients with HBV/HIV coinfection or when HBV resistance develops: Patients with HBV/HIV coinfection may develop severe hepatic flares. ZDV: Steatosis	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. ATV: Jaundice due to indirect hyperbilirubinemia	DTG: Persons with HBV or HCV coinfection may be at higher risk of DTG-associated hepatotoxicity.	MVC: Hepatotoxicity with or without rash or HSRs has been reported. FTR: Transaminase elevation was seen more commonly in patients with HBV/HCV. Transient elevation of bilirubin observed in clinical trials.	N/A

Table 20. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy

Adverse Effect	Drug Class					
	NRTIs	NNRTIs	PIs	INSTIs	EIs	CI
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 after treatment initiation; 90% of reactions occur within 6 weeks. 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.	N/A

Table 20. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy

Adverse Effect	Drug Class					
	NRTIs	NNRTIs	PIs	INSTIs	EIs	CI
Injection Site Reaction		RPV IM injection: Reported in >80% of patients; reactions may include localized pain/discomfort (most common), nodules, induration, swelling, erythema, hematoma.		CAB IM injection: Reported in >80% of patients; reactions may include localized pain/discomfort (most common), nodules, induration, swelling, erythema, hematoma.	T-20 SQ injection: Reported in almost all patients; reactions may include pain, tenderness, nodules, induration, ecchymosis, erythema.	LEN SQ injection: Reported in 47–62% of patients; reactions may include swelling, erythema, pain, nodules, inflammation, induration. Nodules and induration may persist for months in some patients.
Lactic Acidosis	Reported with older NRTIs, d4T, ZDV, and ddI, but not with ABC, 3TC, FTC, TAF, or TDF.	N/A	N/A	N/A	N/A	N/A
Lipodystrophy	Lipoatrophy: Associated with history of exposure to d4T or ZDV (d4T > ZDV). Not reported with ABC, 3TC or FTC, or TAF or TDF.	Lipohypertrophy: Trunk fat increase is observed with EFV-, PI-, and RAL-containing regimens; however, a causal relationship has not been established.			N/A	N/A
Myopathy/Elevated Creatine Phosphokinase	ZDV: Myopathy	N/A	N/A	RAL and DTG: ↑ CPK, rhabdomyolysis, and myopathy or myositis have been reported.	N/A	N/A

Table 20. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy

Adverse Effect	Drug Class					
	NRTIs	NNRTIs	PIs	INSTIs	EIs	CI
Nervous System/Psychiatric Effects	History of exposure to ddI, ddC, or d4T: Peripheral neuropathy (can be irreversible)	Neuropsychiatric events: EFV > RPV, DOR, ETR EFV: Somnolence, insomnia, abnormal dreams, dizziness, impaired concentration, depression, psychosis, suicidal ideation, ataxia, encephalopathy. Some symptoms may subside or diminish after 2–4 weeks. Bedtime dosing and taking without food may reduce symptoms. Risk factors include psychiatric illness, concomitant use of agents with neuropsychiatric effects, and genetic factors. RPV: Depression, suicidality, sleep disturbances DOR: Sleep disorders and disturbances, dizziness, altered sensorium; depression and suicidality and 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	LEN: Headache
Rash	FTC: Hyperpigmentation	All NNRTIs	ATV, DRV, and LPV/r	All INSTIs	MVC, IBA, FTR	N/A

Table 20. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy

Adverse Effect	Drug Class					
	NRTIs	NNRTIs	PIs	INSTIs	EIs	CI
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. 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 FTR: SCr >1.8 x ULN seen in 19% in a clinical trial, but primarily with underlying renal disease or other drugs known to affect creatinine	N/A
Stevens-Johnson Syndrome/Toxic Epidermal Necrosis	N/A	NVP > EFV, ETR, RPV	Some reported cases for DRV, LPV/r, and ATV	RAL	N/A	N/A
Weight Gain	Weight gain has been associated with initiation of ART and subsequent viral suppression. The increase appears to be greater with INSTIs than with other drug classes. Greater weight increase has also been reported with TAF than with TDF and with DOR than with EFV.			INSTI > other ARV drug classes	N/A	N/A

Key: 3TC = lamivudine; ABC = abacavir; ART= antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/r = atazanavir/ritonavir; BIC = bictegravir; BMD = bone mineral density; CAB = cabotegravir; CD4 = CD4 T lymphocyte; CI = capsid inhibitor; CNS = central nervous system; COBI = cobicistat; CPK = creatine phosphokinase; Cr = creatinine; CVD = cardiovascular disease; d4T = stavudine; ddC = zalcitabine; 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; FTR = fostemsavir; GI = gastrointestinal; HBV = hepatitis B virus; HCV = hepatitis C virus; HDL = high-density lipoprotein; HSR = hypersensitivity reaction; IBA = ibalizumab; IDV = indinavir; IM = intramuscular; INSTI = integrase strand transfer inhibitor; LDL = low-density lipoprotein; LEN = lenacapavir; 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; SQ = subcutaneous; SQV = saquinavir; SQV/r = saquinavir/ritonavir; T-20 = enfuvirtide; TAF = tenofovir alafenamide; TC = total cholesterol; TDF = tenofovir disoproxil fumarate; TG = triglycerides; TPV = tipranavir; TPV/r = tipranavir/ritonavir; ULN = upper limit of normal; ZDV = zidovudine

Table 21. Antiretroviral Therapy-Associated Adverse Effects That Can Be Managed with Substitution of Alternative Antiretroviral Agents

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

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	Regimen not including ZDV	ZDV has been associated with neutropenia and macrocytic anemia.
Calculi Nephrolithiasis and cholelithiasis	ATV, ATV/c, ATV/r	DRV/c, DRV/r, INSTI, or NNRTI	This switch should be made if ATV is the presumed cause of the calculi.
Cardiac QTc Interval Prolongation	EFV, RPV, FTR	Boosted ATV or DRV, DOR, or INSTI-based regimen (that does not combine with RPV)	High EFV, RPV, and FTR 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. For FTR, if there is no alternative ARV drug option, consider switching the concomitant medication.
Cardiovascular Events Myocardial infarction, ischemic stroke	ABC	TDF or TAF	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	INSTI, RPV, or DOR	If lipids are a concern, see Dyslipidemia below. Large observation cohorts have found an association between some PIs (DRV, FPV, IDV, LPV/r) and an increased risk of CV events. However, this association has not been seen with ATV. Further study is needed.
Dyslipidemia	RTV- or COBI-boosted PI,	INSTI, DOR, or RPV	Elevated TG and LDL levels are more common with LPV/r and FPV/r than with other RTV-boosted PIs.

Table 21. Antiretroviral Therapy-Associated Adverse Effects That Can Be Managed with Substitution of Alternative Antiretroviral Agents

Adverse Event	ARV Agent(s) or Drug Class		Comments
	Switch from	Switch to	
Hypertriglyceridemia (with or without elevated LDL level)	EFV-based regimens		Improvements in TG and LDL levels have been observed with switch from LPV/r to ATV or ATV/r.[c]
Gastrointestinal Effects Nausea, diarrhea	LPV/r	Boosted ATV or DRV, INSTI, NNRTI	GI intolerance is common with boosted PIs and is linked to the total dose of RTV. More GI toxicity is seen with LPV/r than with ATV/r or DRV/r. GI effects are often transient and do not warrant ARV substitution unless they are persistent and intolerable.
	Other RTV- or COBI-boosted regimens	BIC, DTG, RAL, or NNRTI	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	Any appropriate ABC-sparing regimen	Never rechallenge with ABC following a suspected HSR, regardless of the patient's HLA-B*5701 status.
	EFV, ETR, NVP, RPV	Non-NNRTI ART	Risk of HSR with NVP is higher for women and those with high CD4 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	INSTI, NNRTI	Results of switch studies have been inconsistent. Studies in HIV-negative patients suggest a direct causal effect of LPV/r on insulin resistance. However, traditional risk factors for insulin resistance may be stronger risk factors than the use of any PI.
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	Peripheral lipoatrophy (loss of subcutaneous fat of the limbs, face, and buttocks) is associated with prior thymidine analog (d4T and ZDV) use. Despite switching from these ARVs, fat recovery remains slow (may take years) and incomplete.		
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 lipohypertrophy.		
Neuropsychiatric Side Effects Dizziness, suicidal ideation, abnormal dreams, depression, ataxia, encephalopathy	EFV, RPV	DOR, 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, but in some patients, ataxia or encephalopathy may appear months to years after EFV-initiation. Persistent or intolerable effects should prompt substitution of EFV. INSTIs are associated with insomnia. Depression and suicidality have been infrequently reported with INSTI use, primarily in patients with pre-existing psychiatric conditions.
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

Table 21. Antiretroviral Therapy-Associated Adverse Effects That Can Be Managed with Substitution of Alternative Antiretroviral Agents

Adverse Event	ARV Agent(s) or Drug Class		Comments
	Switch from	Switch to	
			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.
Renal Effects Including proximal renal tubulopathy and elevated creatinine	TDF[a]	ABC,[b] TAF (for patients with CrCl >30 mL/min, unless on chronic hemodialysis), 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	BIC, DTG, EVG/c/TAF/FTC, RAL, boosted DRV, 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.

[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: 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; FTR = fostemsavir; 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 22a. Insurance and Health Program Prescription Drug Pricing and Access

Insurance/Health Program	Prescription Drug Pricing and Access
Medicaid	Drug manufacturers must participate in the MDRP for their drugs to be covered by Medicaid and under Medicare Part B. Manufacturers are required to pay Medicaid programs a rebate of at least 23.1% of the AMP for most brand-name drugs (13% for generics) sold to retail pharmacies or outpatient care providers (notably infused, injected, implanted, inhaled, or instilled drugs). Manufacturers pay additional rebates if this confidential AMP increases faster than the CPI-U rate of inflation. Additionally, many states negotiate with manufacturers for supplemental rebates. States are permitted to require "nominal" cost sharing for medical and pharmacy benefits for some beneficiaries, although many elect not to do so. States can obtain a waiver to allow them to apply higher cost sharing.
Medicare	ARVs are one of six "protected drug classes" under Medicare Part D. Part D plans must provide access to all, or substantially all, FDA-approved ARVs. Part-D plan sponsors, or PBMs on their behalf, negotiate rebates on outpatient drugs with manufacturers; the extent of rebating is unclear. Most physician-administered drugs and biologics are covered under Medicare Part B at a set cost: ASP plus 6%. This pricing mechanism controls spending by narrowing the spread between what is actually paid for the drug and what is actually billed to Medicare. Premiums and cost-sharing payments may be significant for both services and prescription drugs; Part A (hospital care) and Part B place no cap on out-of-pocket spending. Some subsidies and supplemental coverage are offered for low-income beneficiaries. Manufacturer copay assistance programs cannot be applied to Part B or Part D cost sharing; cost-sharing support is available from ADAPs, foundations, and other sources and is based on financial eligibility criteria.
Commercial Insurance	Private insurance plans, or PBMs on their behalf, negotiate rebates on inpatient and outpatient drugs with manufacturers; the extent of rebating is unclear. Formulary restrictions and utilization management (prior authorization, step therapy, higher cost sharing) involving drugs and biologics covered under plans' pharmacy benefit or medical benefit (e.g., infused or injected ARVs) are possible cost-containment measures. Cost sharing can be highly variable. Manufacturer copay assistance programs can be applied in most cases but may not count toward annual ACA cost-sharing limits; cost-sharing support is also available from ADAPs, foundations, and other sources and is based on financial eligibility criteria.
ADAPs	Significant discounting on most ARVs negotiated by the ADAP Crisis Task Force is allowed under the 340B Drug Pricing Program. There is usually no cost sharing for ADAP clients who are uninsured. ADAP can assist with commercial or public insurance out-of-pocket costs.
Veterans Affairs	The FCP is the maximum price manufacturers may charge the four largest federal purchasers of pharmaceuticals (the "Big Four"): The Department of Veterans Affairs (VA), Department of Defense, Public Health Service (including the Indian Health Service), and the Coast Guard. The FCP of a drug includes a 24% discount on a drug's average price paid by non-federal purchasers. Additional discounts may be applied if non-federal purchase prices increase faster than the CPI-U inflation rate. Big Four prices may be 40% to 50% below list prices. The VA may negotiate further price reductions. Prescription drug cost sharing is generally nominal; medications are not withheld from those who cannot afford cost-sharing expenses.

Table 22a. Insurance and Health Program Prescription Drug Pricing and Access

Insurance/Health Program	Prescription Drug Pricing and Access
Community Health Centers	Many community health centers are enrolled in the 340B Drug Pricing Program, which allows discounted drug purchasing using the MDRP formula. Discounts start at 23.1% off AMP, with additional discounts if the AMP increases faster than the CPI-U rate of inflation. Cost sharing in community health centers is first driven by payer source. For clients who are uninsured, cost sharing, if required, is typically based on a sliding fee scale.

Key: ACA = Affordable Care Act; ADAP = AIDS Drug Assistance Program; AMP = average manufacturer price; ARV = antiretroviral; ASP = average sales price; CPI-U = consumer price index-urban; FCP = federal ceiling price; FDA = U.S. Food and Drug Administration; MDRP = Medicaid Drug Rebate Program; PBM = pharmacy benefits manager

Table 22b. Monthly Average Prices of Commonly Used Antiretroviral Drugs

Table 22b includes three benchmark prices, rounded to the nearest dollar, for commonly used 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 payers regarding actual prices, comparative cost savings, formulary restrictions, and patient cost-sharing requirements. **WAC** is the list price published by manufacturers for prescription drugs or biologics sold to wholesalers. The WAC price approximates what retail pharmacies pay wholesalers for single-source (e.g., brand-name) drugs. There is a range of WAC prices for generic ARV drugs, because these are multiple-source products with variable list prices. With increasing competition, actual transactional prices of generic drugs decrease substantially among wholesalers and pharmacies. **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 includes variable price concessions along supply and payment chains, including discounts and rebates to wholesalers, pharmacies, federal purchasers (e.g., the Department of Veterans Affairs), pharmacy benefit managers, commercial insurers, Medicaid, 340B pharmacies, and ADAPs. The availability of these discounts and rebates depends on product demand, market competition, and WAC price increases set by manufacturers. Maximum Medicaid payment rates are assigned to generic products with three or more therapeutically and pharmaceutically equivalent products, as determined by the U.S. Food and Drug Administration. This federally established pharmacy reimbursement limit is the **FUL**. Federal Medicaid will reimburse state Medicaid programs up to this limit for multiple-source drugs (plus the dispensing fee); states may set their own **SMACs** and commercial insurers set their own reimbursement upper limits with pharmacies. Whereas WACs and AWPs are generally set annually, FULs are adjusted on a monthly basis, particularly for multiple-source drugs with fluctuating pharmacy acquisition costs. In this table, 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 (Monthly, Unless Otherwise Noted)	WAC (Monthly, Unless Otherwise Noted)[b]	AWP (Monthly, Unless Otherwise Noted)[b]	FUL (As of February 28, 2023)[c]
NRTIs					
Abacavir					
Generic	300-mg tablet	60 tablets	$100 to $150	$578 to $603	$25
Ziagen	300-mg tablet	60 tablets	$559	$670	
Emtricitabine					
Generic	200-mg capsule	30 capsules	$464	$579	Pending
Emtriva	200-mg capsule	30 capsules	$537	$644	
Lamivudine					
Generic	300-mg tablet	30 tablets	$75 to $343	$324 to $430	$51
Epivir	300-mg tablet	30 tablets	$416	$499	

Table 22b. Monthly Average Prices of Commonly Used Antiretroviral Drugs

ARV Drug (Generic and Brand Names)	Strength, Formulation	Tablets, Capsules, or mLs (Monthly, Unless Otherwise Noted)	WAC (Monthly, Unless Otherwise Noted)[b]	AWP (Monthly, Unless Otherwise Noted)[b]	FUL (As of February 28, 2023)[c]
Tenofovir Disoproxil Fumarate					
Generic	300-mg tablet	30 tablets	$27 to $142	$167 to $1,216	$50
Viread	300-mg tablet	30 tablets	$1,254	$1,504	
Zidovudine					
Generic	300-mg tablet	60 tablets	$36 to $54	$54 to $365	$13
NRTI Combination Products					
Abacavir/Lamivudine					
Generic	600-mg/300-mg tablet	30 tablets	$185 to $1,116	$1,393 to $1,395	$59
Epzicom	600-mg/300-mg tablet	30 tablets	$1,292	$1,550	
Tenofovir Alafenamide/Emtricitabine					
Descovy	25-mg/200-mg tablet	30 tablets	$2,159	$2,591	N/A
Tenofovir Disoproxil Fumarate/Emtricitabine					
Generic	300-mg/200-mg tablet	30 tablets	$25 to $853	$70 to $2,100	$17
Truvada	300-mg/200-mg tablet	30 tablets	$1,842	$2,211	
Tenofovir Disoproxil Fumarate/Lamivudine					
Cimduo	300-mg/300-mg tablet	30 tablets	$1,129	$1,354	N/A
Zidovudine/Lamivudine					
Generic	300-mg/150-mg tablet	60 tablets	$125 to $578	$265 to $932	$55
Combivir	300-mg/150-mg tablet	60 tablets	$901	$1,082	
Abacavir Sulfate/Zidovudine/Lamivudine					
Trizivir	300-mg/300-mg/150-mg tablet	60 tablets	$1,610	$1,932	N/A
NNRTIs					
Efavirenz					
Generic	600-mg tablet	30 tablets	$80 to $980	$1,073 to $1,117	$215

Table 22b. Monthly Average Prices of Commonly Used Antiretroviral Drugs

ARV Drug (Generic and Brand Names)	Strength, Formulation	Tablets, Capsules, or mLs (Monthly, Unless Otherwise Noted)	WAC (Monthly, Unless Otherwise Noted)[b]	AWP (Monthly, Unless Otherwise Noted)[b]	FUL (As of February 28, 2023)[c]
Sustiva	600-mg tablet	30 tablets	$981	$1,177	
Doravirine					
Pifeltro	100-mg tablet	30 tablets	$1,677	$2,012	N/A
Etravirine					
Generic	200-mg tablet	60 tablets	$1,287	$1,609	$1,154
Intelence	200-mg tablet	60 tablets	$1,469	$1,762	
Nevirapine					
Generic	200-mg tablet	60 tablets	$10 to $45	$648 to $651	$47
Generic XR	400-mg tablet	30 tablets	$135 to $565	$595 to $706	$149
Viramune XR	400-mg tablet	30 tablets	$840	$1,008	
Rilpivirine					
Edurant	25-mg tablet	30 tablets	$1,350	$1,620	N/A
PIs					
Atazanavir					
Generic	200-mg capsule	60 capsules	$178 to $800	$1,517 to $1,668	$711
Reyataz	200-mg capsule	60 capsules	$1,463	$1,756	
Generic	300-mg capsule	30 capsules	$178 to $1,018	$1,502 to $1,652	$187
Reyataz	300-mg capsule	30 capsules	$1,449	$1,739	
Atazanavir/Cobicistat					
Evotaz	300-mg/150-mg tablet	30 tablets	$1,605	$1,927	N/A
Darunavir					
Prezista	600-mg tablet	60 tablets	$2,095	$2,514	N/A
Prezista	800-mg tablet	30 tablets	$2,095	$2,514	N/A
Prezista	100-mg/mL suspension	200 mL	$2,095	$2,514	N/A

Table 22b. Monthly Average Prices of Commonly Used Antiretroviral Drugs

ARV Drug (Generic and Brand Names)	Strength, Formulation	Tablets, Capsules, or mLs (Monthly, Unless Otherwise Noted)	WAC (Monthly, Unless Otherwise Noted)[b]	AWP (Monthly, Unless Otherwise Noted)[b]	FUL (As of February 28, 2023)[c]
Darunavir/Cobicistat					
Prezcobix	800-mg/150-mg tablet	30 tablets	$2,395	$2,874	N/A
Lopinavir/Ritonavir					
Generic	200-mg/50-mg tablet	120 tablets	$885	$1,106	Pending
Kaletra	200-mg/50-mg tablet	120 tablets	$1,024	$1,229	
Tipranavir					
Aptivus	250-mg capsule	120 capsules	$1,995	$2,394	N/A
INSTIs					
Dolutegravir					
Tivicay	50-mg tablet	30 tablets	$2,131	$2,557	N/A
Tivicay	50-mg tablet	60 tablets	$4,262	$5,114	N/A
Raltegravir					
Isentress	400-mg tablet	60 tablets	$1,910	$2,292	N/A
Isentress HD	600-mg tablet	60 tablets	$1,910	$2,202	N/A
Fusion Inhibitor					
Enfuvirtide					
Fuzeon	90-mg injection kit	60 doses (1 kit)	$3,586	$4,303	N/A
CCR5 Antagonist					
Maraviroc					
Generic	150-mg tablet	60 tablets	$1,141	$1,764	Pending
Selzentry	150-mg tablet	60 tablets	$1,730	$2,076	
Generic	300-mg tablet	60 tablets	$1,141	$1,764	Pending
Selzentry	300-mg tablet	60 tablets	$1,730	$2,076	
Selzentry	300-mg tablet	120 tablets	$3,460	$4,152	N/A

Table 22b. Monthly Average Prices of Commonly Used Antiretroviral Drugs

ARV Drug (Generic and Brand Names)	Strength, Formulation	Tablets, Capsules, or mLs (Monthly, Unless Otherwise Noted)	WAC (Monthly, Unless Otherwise Noted)[b]	AWP (Monthly, Unless Otherwise Noted)[b]	FUL (As of February 28, 2023)[c]
CD4-Directed Post-Attachment Inhibitor					
Ibalizumab-uiyk					
Trogarzo	200-mg vial	8 vials	$11,452	$13,740	N/A
gp120-Directed Attachment Inhibitor					
Fostemsavir					
Rukobia	600-mg tablet	60 tablets	$8,505	$10,206	N/A
Capsid Inhibitor					
Lenacapavir					
Sunlenca	300-mg tablet	4 tablets	$3,250	$3,900	N/A
Sunlenca	300-mg tablet	5 tablets	$4,063	$4,875	N/A
Sunlenca	927-mg injection kit	2 vials (1 kit every 6 months)	$19,500 (every 6 months)	$23,400 (every 6 months)	N/A
Coformulated Combination Products as Single-Tablet Regimens					
Bictegravir/Tenofovir Alafenamide/Emtricitabine					
Biktarvy	50-mg/25-mg/200-mg tablet	30 tablets	$3,795	$4,554	N/A
Darunavir/Cobicistat/Tenofovir Alafenamide/Emtricitabine					
Symtuza	800-mg/150-mg/10-mg/200-mg tablet	30 tablets	$4,593	$5,511	N/A
Dolutegravir/Abacavir/Lamivudine					
Triumeq	50-mg/600-mg/300-mg tablet	30 tablets	$3,537	$4,225	N/A
Dolutegravir/Lamivudine					
Dovato	50-mg/300-mg tablet	30 tablets	$2,810	$3,372	N/A
Dolutegravir/Rilpivirine					
Juluca	50-mg/25-mg tablet	30 tablets	$3,315	$3,978	N/A
Doravirine/Tenofovir Disoproxil Fumarate/Lamivudine					

Table 22b. Monthly Average Prices of Commonly Used Antiretroviral Drugs

ARV Drug (Generic and Brand Names)	Strength, Formulation	Tablets, Capsules, or mLs (Monthly, Unless Otherwise Noted)	WAC (Monthly, Unless Otherwise Noted)[b]	AWP (Monthly, Unless Otherwise Noted)[b]	FUL (As of February 28, 2023)[c]
Delstrigo	100-mg/300-mg/300-mg tablet	30 tablets	$2,552	$3,063	N/A
Efavirenz/Tenofovir Disoproxil Fumarate/Emtricitabine					
Generic	600-mg/300-mg/200-mg tablet	30 tablets	$120 to $252	$302 to $3,414	$151
Atripla	600-mg/300-mg/200-mg tablet	30 tablets	$2,995	$3,594	
Efavirenz/Tenofovir Disoproxil Fumarate/Lamivudine					
Symfi	600-mg/300-mg/150-mg tablet	30 tablets	$1,835	$2,201	N/A
Symfi Lo	400-mg/300-mg/150-mg tablet	30 tablets	$1,835	$2,201	N/A
Elvitegravir/Cobicistat/Tenofovir Alafenamide/Emtricitabine					
Genvoya	150-mg/150-mg/10-mg/ 200-mg tablet	30 tablets	$3,795	$4,554	N/A
Elvitegravir/Cobicistat/Tenofovir Disoproxil Fumarate/Emtricitabine					
Stribild	150-mg/150-mg/300-mg/ 200-mg tablet	30 tablets	$3,981	$4,777	N/A
Rilpivirine/Tenofovir Alafenamide/Emtricitabine					
Odefsey	25-mg/25-mg/200-mg tablet	30 tablets	$3,454	$4,145	N/A
Rilpivirine/Tenofovir Disoproxil Fumarate/Emtricitabine					
Complera	25-mg/300-mg/200-mg tablet	30 tablets	$3,454	$4,145	N/A
Copackaged Combination Products as Injectable Regimens					
Cabotegravir + Rilpivirine					
Cabenuva	600 mg (3 mL) 900 mg (3 mL)	2 vials (every other month)	$6,334 (every other month)	$7,601 (every other month)	NA
Cabenuva	400 mg (2 mL) 600 mg (2 mL)	2 vials	$4,223	$5,067	NA
PK Enhancers (Boosters)					
Cobicistat					

Table 22b. Monthly Average Prices of Commonly Used Antiretroviral Drugs

ARV Drug (Generic and Brand Names)	Strength, Formulation	Tablets, Capsules, or mLs (Monthly, Unless Otherwise Noted)	WAC (Monthly, Unless Otherwise Noted)[b]	AWP (Monthly, Unless Otherwise Noted)[b]	FUL (As of February 28, 2023)[c]
Tybost	150-mg tablet	30 tablets	$283	$340	N/A
Ritonavir					
Generic	100-mg tablet	30 tablets	$80 to $160	$278	$75
Norvir	100-mg tablet	30 tablets	$257	$309	

[a] The following less commonly used ARV drugs are not included in this table: fosamprenavir and nelfinavir.

[b] Source: Micromedex Red Book [database]. IBM Watson Health. 2023. Available at: https://www.micromedexsolutions.com.

[c] Source: Federal Upper Limits–March 2023 [database]. Medicare & Medicaid Services. 2023. Available at: https://www.medicaid.gov/medicaid/prescription-drugs/pharmacy-pricing/index.html.

Key: ADAP = AIDS Drug Assistance Program; ARV = antiretroviral; AWP = average wholesale price; CD4 = CD4 T lymphocyte; FUL = federal upper limit; HD = high dose; INSTI = integrase strand transfer inhibitor; N/A = not applicable; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PK = pharmacokinetic; SMAC = state maximum allowable cost; WAC = wholesale acquisition cost; XR = extended release

Table 23. Mechanisms of Antiretroviral-Associated Drug Interactions

Pharmacokinetic interactions may occur during absorption, metabolism, or elimination of the antiretroviral (ARV) drug and/or the interacting drug. This table does not include a comprehensive list of all possible mechanisms of interactions for individual ARV drugs (e.g., transporters); however, the table lists the most common mechanisms of known interactions and focuses on absorption and cytochrome P 450 (CYP)– and uridine diphosphate glucuronosyltransferase (UGT) 1A1–mediated interactions.

Note: N/A indicates that there are no clinically relevant interactions by the mechanism. Identified mechanisms are specific to the ARV drugs described in the row and may not be reflective of complete ARV regimens. The older ARVs—fosamprenavir, nelfinavir, tipranavir, and zidovudine—are not commonly used in clinical practice and are **not** included in this table. Please refer to the U.S. Food and Drug Administration product labels for these ARVs for information regarding drug interactions.

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			
	Increasing Gastric pH	Cationic Chelation	P-gp	CYP Substrate	CYP Inhibitor	CYP Inducer	UGT1A1
INSTIs							
BIC	N/A	Concentrations of PO INSTIs are decreased by products that contain polyvalent cations (e.g., Ca, Mg, Al, Fe, Zn).	Substrate	3A4	N/A	N/A	Substrate
CAB	N/A		Substrate	N/A	N/A	N/A	Substrate
DTG	N/A		Substrate	3A4 (minor)	N/A	N/A	Substrate
EVG/c	N/A		Inhibitor	3A4	3A4, 2D6	2C9	Substrate
RAL	N/A		N/A	N/A	N/A	N/A	Substrate
PIs							
ATV	Concentration decreased	N/A	Substrate, Inducer, Inhibitor	3A4	3A4, 2C8	N/A	Inhibitor
ATV/c	Concentration decreased	N/A	Substrate, Inhibitor	3A4	3A4, 2D6, 2C8	N/A	Inhibitor
ATV/r	Concentration decreased	N/A	Substrate, Inhibitor	3A4, 2D6	3A4, 2D6, 2C8	1A2, 2B6, 2C8, 2C9, 2C19	ATV: Inhibitor RTV: Inducer

Table 23. Mechanisms of Antiretroviral-Associated Drug Interactions

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			
	Increasing Gastric pH	Cationic Chelation	P-gp	CYP Substrate	CYP Inhibitor	CYP Inducer	UGT1A1
PIs (continued)							
DRV/c	N/A	N/A	Substrate, Inhibitor	3A4	3A4, 2D6	N/A	No data
DRV/r	N/A	N/A	Substrate, Inhibitor	3A4, 2D6	3A4, 2D6	1A2, 2B6, 2C8, 2C9, 2C19	Inducer
LPV/r	N/A	N/A	Substrate	3A4, 2D6	3A4	1A2, 2B6, 2C8, 2C9, 2C19	Inducer
NNRTIs							
DOR	N/A	N/A	N/A	3A4, 3A5	N/A	N/A	N/A
EFV	N/A	N/A	N/A	2B6 (primary), 2A6, 3A4	3A4	3A4, 2B6, 2C19	N/A
ETR	N/A	N/A	N/A	3A4, 2C9, 2C19	2C9, 2C19	3A4	N/A
NVP	N/A	N/A	N/A	3A4, 2B6	N/A	3A4, 2B6	N/A
RPV	Only RPV PO: Concentration decreased	N/A	N/A	3A4	N/A	N/A	N/A
NRTIs							
ABC	N/A	N/A	N/A	N/A	N/A	N/A	N/A
FTC	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
TAF	N/A	N/A	Substrate	N/A	N/A	N/A	N/A
TDF	N/A	N/A	Substrate	N/A	N/A	N/A	N/A
Capsid Inhibitor							
LEN (SQ and PO)	N/A	N/A	Substrate	3A4	3A4	N/A	Substrate
CCR5 Antagonist							
MVC	N/A	N/A	Substrate	3A4	N/A	N/A	N/A

Table 23. Mechanisms of Antiretroviral-Associated Drug Interactions

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			
	Increasing Gastric pH	Cationic Chelation	P-gp	CYP Substrate	CYP Inhibitor	CYP Inducer	UGT1A1
gp120-Directed Attachment Inhibitor							
FTR	N/A	N/A	Substrate	3A4	N/A	N/A	N/A
Fusion Inhibitor							
T-20	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Post-Attachment Inhibitor							
IBA	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Key: 3TC = lamivudine; ABC = abacavir; Al = aluminum; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; Ca = calcium; CAB = cabotegravir; CYP = cytochrome P; DOR = doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; Fe = iron; FTC = emtricitabine; FTR = fostemsavir; IBA = ibalizumab; INSTI = integrase strand transfer inhibitor; LEN = lenacapavir; LPV/r = lopinavir/ritonavir; Mg = magnesium; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitors; NRTI = nucleoside reverse transcriptase inhibitors; NVP = nevirapine; P-gp = P-glycoprotein; PI = protease inhibitor; PO = oral; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQ = subcutaneous; T-20 = enfuvirtide; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; UGT = uridine diphosphate glucuronosyltransferase; Zn = zinc

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

This table provides information on the known or predicted interactions between protease inhibitors (PIs) and non-antiretroviral (ARV) drugs. When information is available, interactions for boosted atazanavir (ATV) (with either ritonavir [RTV] or cobicistat [COBI]) and unboosted ATV are listed separately. The term "all PIs" refers to both unboosted ATV and ATV, darunavir (DRV), and lopinavir (LPV) boosted with either RTV or COBI. This table does not include interactions for fosamprenavir (FPV), nelfinavir (NFV), or tipranavir (TPV). For information regarding interactions between PIs and other ARV drugs, including dosing recommendations, refer to Tables 24c, 25a, and 25b.

Recommendations for managing a particular drug interaction may differ depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or whether a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgement to select the most appropriate alternative medication to use.

Note: FPV, NFV, and TPV are no longer commonly used in clinical practice and are **not** included in this table. Please refer to the U.S. Food and Drug Administration product labels for information regarding drug interactions between these PIs and concomitant medications.

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers			
Antacids	ATV (unboosted), ATV/c, ATV/r	When Given Simultaneously • ↓ ATV expected	Administer ATV at least 2 hours before or 2 hours after antacids or buffered medications.
H2 Receptor Antagonists	ATV (unboosted)	When Given Simultaneously With Famotidine • ATV AUC ↓ 41% When Given 2 Hours Before and **≥10** Hours After H2RA • ↔ ATV	A single dose of H2RA should not exceed a dose equivalent to famotidine 20 mg, and the total daily dose should not exceed a dose equivalent to famotidine 20 mg twice daily in PI-naive patients. Give ATV with food at least 2 hours before and at least 10 hours after the H2RA. Do not coadminister unboosted ATV plus H2RA in PI-experienced patients.
	ATV/c, ATV/r	↓ ATV expected	H2RA dose should not exceed a dose equivalent to famotidine 40 mg twice daily in ART-naive patients or famotidine 20 mg twice daily in ART-experienced patients.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
			Give ATV 300 mg (plus COBI 150 mg or RTV 100 mg) with food simultaneously with and/or ≥10 hours after the dose of H2RA. If using TDF and H2RA in ART-experienced patients, administer ATV 400 mg plus RTV 100 mg with food simultaneously with and/or ≥10 hours after the dose of H2RA. Do not coadminister ATV/c with TDF and H2RA in ART-experienced patients.
	DRV/c, DRV/r, LPV/r	With Ranitidine • ↔ DRV/r ↔ PI expected	No dose adjustment needed.
Proton Pump Inhibitors	ATV (unboosted)	With Omeprazole 40 mg • ATV AUC ↓ 94%	Do not coadminister.
	ATV/c, ATV/r	With Omeprazole 40 mg • ATV AUC ↓ 76% When Omeprazole 20 mg Is Given 12 Hours Before ATV/c or ATV/r • ATV AUC ↓ 42%	PPI dose should not exceed a dose equivalent to omeprazole 20 mg daily in PI-naive patients. PPIs should be administered at least 12 hours before ATV/c or ATV/r. Do not coadminister in PI-experienced patients.
	DRV/c, LPV/r	↔ PI expected	No dose adjustment needed.
	DRV/r	↔ DRV/r Omeprazole AUC ↓ 42%	Consider alternative ARV or acid reducer. If coadministered, monitor for omeprazole efficacy. If the patient does not experience symptomatic relief, increase the dose to no more than omeprazole 40 mg daily.
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/adverse events. Dose reduction may be necessary.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Tamsulosin	All PIs	↑ tamsulosin expected	**Do not coadminister unless benefits outweigh risks.** If coadministered, monitor for tamsulosin-related adverse events.
Terazosin	All PIs	↔ or ↑ terazosin possible	Initiate terazosin at lowest dose and titrate while monitoring for clinical response/adverse events. Dose reduction may be necessary.
Silodosin	All PIs	↑ silodosin expected	**Contraindicated.**
Antibacterials—Antimycobacterials			
Bedaquiline	All PIs	With LPV/r • Bedaquiline AUC ↑ 1.9-fold With Other PI/r, ATV/c, or DRV/c • ↑ bedaquiline possible	**Do not coadminister unless benefits outweigh risks.** Monitor liver function and ECG for QTc prolongation.
Rifabutin	ATV (unboosted)	↑ rifabutin AUC expected	Recommended dose is rifabutin 150 mg once daily. Monitor for antimycobacterial activity and consider therapeutic drug monitoring. Monitor for rifabutin-related adverse events, including neutropenia and uveitis. PK data in this table are results from healthy volunteer studies. Lower rifabutin exposure has been reported in patients with HIV than in healthy study participants.
	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%	

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	PI/c	↑ rifabutin expected ↓ COBI expected	Do not coadminister.
Rifampin	All PIs	↓ PI concentration by >75%	Contraindicated. Increasing the dose of RTV does not overcome this interaction and may increase hepatotoxicity. Increasing the COBI dose is not recommended. Consider rifabutin if a rifamycin is indicated.
Rifapentine	All PIs	↓ PI expected	Do not coadminister.
Antibacterials—Macrolides			
Azithromycin	ATV (unboosted), ATV/c, ATV/r	↑ azithromycin possible	No dose adjustment needed.
	DRV/c, DRV/r	↔ azithromycin expected	No dose adjustment needed.
Clarithromycin	ATV (unboosted)	Clarithromycin AUC ↑ 94% ATV ↑ 28%	Reduce clarithromycin dose by 50% or consider alternative ARV or azithromycin. Monitor for clarithromycin-related adverse events, including QTc prolongation.
	ATV/r, PI/c	↑ clarithromycin expected ↑ ATV/r and PI/c expected	Consider alternative ARV or azithromycin.
	DRV/r, LPV/r	DRV/r ↑ clarithromycin AUC 57% LPV/r ↑ clarithromycin expected RTV 500 mg twice daily ↑ clarithromycin 77%	Consider alternative ARV or azithromycin. If use of clarithromycin is necessary in a patient with impaired renal function, reduce clarithromycin dose by 50% in patients with CrCl 30 to 60 mL/min. In patients with CrCl <30 mL/min, reduce clarithromycin dose by 75%. Monitor for clarithromycin-related adverse events, including QTc prolongation.
Erythromycin	All PIs	↑ erythromycin expected ↑ PIs expected	Consider alternative ARV or use azithromycin.
Anticoagulants			

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Apixaban	ATV (unboosted)	↑ apixaban possible	No data available for dose recommendation. Consider alternative ARV or anticoagulant.
	PI/c, PI/r	↑ apixaban expected	Do not coadminister in patients who require apixaban 2.5 mg twice daily. In Patients Requiring Apixaban 5 mg or 10 mg Twice Daily • Reduce apixaban dose by 50%.
Dabigatran	ATV (unboosted), DRV/c, DRV/r, LPV/r	No data	No data available for dose recommendation. Consider alternative ARV or anticoagulant.
	ATV/c, ATV/r	With COBI 150 mg Alone • Dabigatran AUC ↑ 110% to 127% With ATV/r • ↑ dabigatran expected	Dabigatran dosing recommendation depends on indication and renal function. Refer to dabigatran prescribing information for dosing instructions when using dabigatran concomitantly with P-glycoprotein inhibitors.
Edoxaban	ATV (unboosted), DRV/c, DRV/r, LPV/r	No data	No data available for dose recommendation. Consider alternative ARV or anticoagulant.
	ATV/r, ATV/c	↑ edoxaban expected	Stroke Prevention in Nonvalvular Atrial Fibrillation Indication • No dose adjustment needed. Deep Venous Thrombosis and Pulmonary Embolism Indication • Administer edoxaban 30 mg once daily.
Rivaroxaban	ATV (unboosted)	↑ rivaroxaban possible	No data available for dose recommendation. Consider alternative ARV or anticoagulant.
	PI/c, PI/r	↑ rivaroxaban expected	Do not coadminister.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Warfarin	PI/c	No data	Monitor INR closely when stopping or starting PI/c or PI/r 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/r	↓ warfarin possible	
Anticonvulsants			
Carbamazepine	ATV (unboosted)	May ↓ PI concentrations substantially	Do not coadminister.
	ATV/r, LPV/r	↑ carbamazepine possible May ↓ PI concentrations substantially	Consider alternative ARV or anticonvulsant. If coadministration is necessary, consider monitoring concentrations of both drugs and assess virologic response. Carbamazepine dose reduction may be necessary. Do not coadminister with LPV/r once daily.
	DRV/r	Carbamazepine AUC ↑ 45% ↔ DRV	Monitor anticonvulsant concentration and adjust dose accordingly.
	PI/c	↑ carbamazepine possible ↓ COBI expected ↓ PI expected	Contraindicated.
Eslicarbazepine	All PIs	↓ PI possible	Consider alternative ARV or anticonvulsant. If coadministration is necessary, monitor for virologic response. Consider monitoring anticonvulsant and PI concentrations.
Ethosuximide	All PIs	↑ ethosuximide possible	Monitor for ethosuximide-related adverse events.
Lamotrigine	ATV (unboosted)	↔ lamotrigine	No dose adjustment needed.
	ATV/r	Lamotrigine AUC ↓ 32%	A dose increase of lamotrigine may be needed; monitor lamotrigine concentration or consider alternative ARV or anticonvulsant.
	LPV/r	Lamotrigine AUC ↓ 50% ↔ LPV	

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	DRV/r	↓ lamotrigine possible	
	PI/c	No data	Monitor anticonvulsant concentration and adjust dose accordingly.
Oxcarbazepine	All PIs	↓ PI possible	Consider alternative ARV or anticonvulsant. If coadministration is necessary, monitor for virologic response. Consider monitoring anticonvulsant and PI concentrations.
Phenobarbital	ATV (unboosted)	↓ ATV expected	Do not coadminister.
	ATV/r, DRV/r	↓ phenobarbital possible ↓ PI possible	Consider alternative anticonvulsant. If coadministration is necessary, consider monitoring concentrations of both drugs and assessing virologic response.
	LPV/r	↓ phenobarbital possible ↓ LPV/r possible	Do not coadminister with LPV/r once daily. Consider alternative anticonvulsant. If coadministration is necessary, consider monitoring concentrations of both drugs and assessing virologic response.
	PI/c	↓ COBI expected ↓ PI expected	Contraindicated.
Phenytoin	ATV (unboosted)	↓ ATV expected	Do not coadminister.
	ATV/r, DRV/r	↓ phenytoin possible ↓ PI possible	Consider alternative anticonvulsant. If coadministration is necessary, consider monitoring concentrations of both drugs and assessing virologic response.
	LPV/r	Phenytoin AUC ↓ 31% LPV/r AUC ↓ 33%	Do not coadminister with LPV/r once daily. Consider alternative anticonvulsant or monitor concentrations of both drugs and assess virologic response.
	PI/c	↓ COBI expected ↓ PI expected	Contraindicated.
Valproic Acid	All PIs	↓ or ↔ VPA possible	Monitor VPA concentrations and monitor for PI tolerability.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
		LPV AUC ↑ 38% No data for other PIs	
Antidepressants, Anxiolytics, and Antipsychotics Also see the Sedative/Hypnotics section below			
Bupropion	ATV (unboosted)	↔ bupropion expected	No dose adjustment needed.
	ATV/r, DRV/r	↓ bupropion possible	Titrate bupropion dose based on clinical response.
	LPV/r	Bupropion AUC ↓ 57%	
	PI/c	↔ bupropion expected	No dose adjustment needed.
Buspirone	All PIs	↑ buspirone expected	Administer lowest dose of buspirone with caution and titrate buspirone dose based on clinical response. Dose reduction may be necessary. Monitor for buspirone-related adverse events.
Nefazodone	All PIs	↑ nefazodone expected ↑ PI possible	Monitor for nefazodone-related adverse events and PI tolerability.
Trazodone	All PIs	RTV 200 mg twice daily (for 2 days) • Trazodone ↑ AUC 240%	Administer lowest dose of trazodone and monitor for CNS and CV adverse events.
Tricyclic Antidepressants Amitriptyline, amoxapine, clomipramine, desipramine, doxepin, imipramine, maprotiline, nortriptyline, protriptyline, trimipramine	All PIs	↑ TCA expected	Administer lowest possible TCA dose and titrate based on clinical assessment and/or drug concentrations. Monitor for TCA-related adverse events.
	DRV/r	Paroxetine AUC ↓ 39%	Titrate SSRI dose based on clinical response.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Selective Serotonin Reuptake Inhibitors		Sertraline AUC ↓ 49%	
(e.g., citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline)	All PIs except DRV/r	No data	Titrate SSRI dose using the lowest available initial or maintenance dose.
Antipsychotics			
Aripiprazole	ATV (unboosted)	↑ aripiprazole expected	Administer 50% of the usual aripiprazole dose. Titrate dose based on clinical monitoring for efficacy/adverse events. Refer to aripiprazole label for doses to use in patients who have major depressive disorder or who are known to be CYP2D6 poor metabolizers.
	PI/c, PI/r	↑ aripiprazole expected	Administer 25% of the usual aripiprazole dose. Titrate dose based on clinical monitoring for efficacy/adverse events. Refer to aripiprazole label for doses to use in patients who have major depressive disorder or who are known to be CYP2D6 poor metabolizers.
Brexpiprazole	ATV (unboosted)	↑ brexpiprazole expected	Administer 50% of the usual brexpiprazole dose. Titrate dose based on clinical monitoring for efficacy/adverse events. Refer to brexpiprazole label for doses to use in patients who have major depressive disorder or who are known to be CYP2D6 poor metabolizers.
	PI/c, PI/r	↑ brexpiprazole expected	Administer 25% of the usual brexpiprazole dose. Titrate the dose based on clinical monitoring for efficacy/adverse events. Refer to brexpiprazole label for doses to use in patients who have major depressive disorder or who are known to be CYP2D6 poor metabolizers.
Cariprazine	All PIs	↑ cariprazine expected	Starting Cariprazine in a Patient Who Is 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 of cariprazine 3 mg daily. If the PI is withdrawn, cariprazine dose may need to be increased. Starting a PI in a Patient Who Is Already Receiving Cariprazine

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
			• For patients receiving cariprazine 3 mg or cariprazine 6 mg daily, reduce the 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, the cariprazine dose may need to be increased.
Iloperidone	All PIs	↑ iloperidone expected	Decrease iloperidone dose by 50%.
Lumateperone	All PIs	↑ lumateperone expected	Do not coadminister.
Lurasidone	ATV (unboosted)	↑ lurasidone expected	Consider alternative ARV or antipsychotic. If coadministration is necessary and atazanavir is added to lurasidone therapy, reduce lurasidone dose by 50%. If coadministration is necessary and lurasidone is added to ATV therapy, the recommended starting dose of lurasidone is 20 mg daily and the maximum recommended dose is 80 mg daily.
	PI/c, PI/r	↑ lurasidone expected	Contraindicated.
Olanzapine	ATV (unboosted), PI/c	↔ olanzapine expected	No dose adjustment needed.
	PI/r	↓ olanzapine possible	Monitor for therapeutic effectiveness of olanzapine.
Other Antipsychotics CYP3A4 and/or CYP2D6 substrates (e.g., clozapine, perphenazine, risperidone, thioridazine)	PI/c, PI/r	↑ antipsychotic possible	Titrate the antipsychotic dose using the lowest initial dose or adjust the maintenance dose accordingly. Monitor for adverse events, including QTc prolongation.
Pimavanserin	ATV (unboosted)	No data	No data available for dose recommendation. Consider alternative ARV or antipsychotic.
	LPV/r	↑ pimavanserin expected	Do not coadminister, due to risk for QTc prolongation.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	All other PIs	↑ pimavanserin expected	Reduce pimavanserin dose to 10 mg once daily.
Pimozide	All PIs	↑ pimozide expected	Contraindicated.
Quetiapine	All PIs	↑ quetiapine expected	Starting Quetiapine in a Patient Receiving a PI • Initiate quetiapine at the lowest dose and titrate up as needed. Monitor for quetiapine effectiveness and adverse events, including QTc prolongation. Starting a PI in a Patient Receiving a Stable Dose of Quetiapine • Consider alternative ARV. If coadministered, reduce quetiapine dose to 1/6 of the current dose. Closely monitor for quetiapine effectiveness and adverse events, including QTc prolongation.
Ziprasidone	LPV/r	↑ ziprasidone expected	Do not coadminister, due to risk for QTc prolongation.
	All other PIs	↑ ziprasidone expected	Monitor for ziprasidone-related adverse events, including QTc prolongation.
Antifungals			
Fluconazole	All PIs	↔ PI expected ↔ fluconazole expected	No dose adjustment needed.
Isavuconazole	LPV/r	Isavuconazole AUC ↑ 96% LPV AUC ↓ 27% RTV AUC ↓ 31%	If coadministered, monitor isavuconazole concentrations and adverse events. Monitor for virologic response.
	All PIs except LPV/r	↑ isavuconazole expected ↑ PI possible	If coadministered, monitor isavuconazole concentrations and monitor for isavuconazole-related adverse events. Monitor for PI tolerability.
Itraconazole	ATV (unboosted)	↑ itraconazole expected	Dose based on itraconazole concentrations and monitor for itraconazole-related adverse events.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	PI/r, PI/c	↑ itraconazole expected ↑ PI expected	Itraconazole doses >200 mg/day **are not recommended** unless dosing is guided by itraconazole concentrations.
Posaconazole	ATV (unboosted)	ATV AUC ↑ 268% ↑ or ↓ posaconazole possible	If coadministered, monitor posaconazole concentrations and monitor for posaconazole-related or PI-related adverse events.
	ATV/r	ATV AUC ↑ 146% ↑ posaconazole possible	
	All other PIs	↑ PI expected ↑ posaconazole possible	
Voriconazole	ATV (unboosted)	↑ or ↓ PI possible ↑ or ↓ voriconazole possible	If coadministered, monitor voriconazole concentrations and monitor for voriconazole-related or PI-related adverse events.
	PI/c	No data	**Do not coadminister** voriconazole and RTV or COBI unless benefits outweigh risks. If coadministered, monitor voriconazole concentration and adjust dose accordingly.
	PI/r	RTV 100 mg twice daily ↓ voriconazole AUC 39%	
Antimalarials			

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Artemether/Lumefantrine	ATV (unboosted), PI/c	↑ lumefantrine expected No data for artemether	Clinical significance is unknown. If coadministered, monitor closely for antimalarial efficacy and lumefantrine-related adverse events, including QTc prolongation.
	DRV/r	Artemether AUC ↓ 16% DHA[a] AUC ↓ 18% Lumefantrine AUC ↑ 175% ↔ DRV	
	LPV/r	Artemether AUC ↓ 40% DHA AUC ↓ 45% Lumefantrine AUC ↑ 4.8-fold ↔ LPV	
Atovaquone/Proguanil	ATV/r, LPV/r	With ATV/r • Atovaquone AUC ↓ 46% • Proguanil AUC ↓ 41% With LPV/r • Atovaquone AUC ↓ 74% • Proguanil AUC ↓ 38%	Clinical significance is unknown. Consider alternative ARV or malaria prophylaxis.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Mefloquine	All PIs	With RTV 200 mg Twice Daily • RTV AUC ↓ 31% and C_{min} ↓ 43% • ↔ mefloquine With ATV (Unboosted), PI/c, or PI/r • No data • ↑ mefloquine possible	Clinical significance is unknown. Consider alternative ARV or antimalarial drug. If coadministered, monitor for mefloquine-related adverse events, including psychiatric symptoms and QTc prolongation. Monitor virologic response.
Antiplatelets			
Clopidogrel	All boosted PIs	Clopidogrel active metabolite AUC ↓ 69% in people with HIV compared to healthy volunteers without HIV. Impaired platelet inhibition observed in people with HIV.	Do not coadminister.
Prasugrel	All boosted PIs	Prasugrel active metabolite AUC ↓ 52% in people with HIV compared to healthy volunteers without HIV. Adequate platelet inhibition observed in people with HIV.	No dose adjustment needed.
Ticagrelor	All PIs	↑ ticagrelor expected	Do not coadminister.
Vorapaxar	All PIs	↑ vorapaxar expected	Do not coadminister.
Antipneumocystis and Antitoxoplasmosis Drug			
Atovaquone Oral suspension	ATV/r	↔ atovaquone	No dose adjustment needed.
	All other PIs	↔ atovaquone expected	No dose adjustment needed.
Antivirals—Orthopoxviruses (Mpox, Smallpox)			
Brincidofovir	All PIs	↑ brincidofovir possible	Give PI dose at least 3 hours after administering brincidofovir and monitor for brincidofovir-related adverse events (i.e., elevations in ALT/AST and bilirubin and GI adverse events).

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Cidofovir	All PIs	↔ cidofovir	No dose adjustment needed.
Tecovirimat	All PIs	↔ tecovirimat	No dose adjustment needed.
Beta-Agonists, Long-Acting Inhaled			
Arformoterol, Formoterol	ATV (unboosted), ATV/c, ATV/r	↑ arformoterol possible	No dose adjustment needed.
	DRV/c, DRV/r, LPV/r	↔ arformoterol expected	No dose adjustment needed.
Indacaterol	All PIs	With RTV 300 mg Twice Daily • Indacaterol AUC ↑ 1.7-fold	No dose adjustment needed in patients receiving indacaterol 75 mcg daily.
Olodaterol	All PIs	↑ olodaterol expected	No dose adjustment needed.
Salmeterol	All PIs	↑ salmeterol possible	Do not coadminister, due to potential increased risk of salmeterol-related CV events.
Cardiac Medications			
Amiodarone	ATV/r	↑ amiodarone possible ↑ PI possible	Contraindicated.
	All other PIs	↑ amiodarone possible ↑ PI possible	Do not coadminister unless the benefits outweigh the risks. If coadministered, monitor for amiodarone-related adverse events and consider monitoring ECG and amiodarone drug concentration.
Antiarrhythmics (e.g., disopyramide, dofetilide, lidocaine, mexiletine, propafenone)	ATV (unboosted)	↑ antiarrhythmic possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor for antiarrhythmic-related adverse events.
	PI/c, PI/r	↑ antiarrhythmic possible	Do not coadminister.
	ATV (unboosted)	↑ dronedarone possible	Do not coadminister.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Dronedarone	PI/c, PI/r	↑ dronedarone expected	Contraindicated.
Flecainide	All PIs	↑ flecainide possible	Do not coadminister.
Propafenone	All PIs	↑ propafenone possible	Do not coadminister.
Quinidine	ATV/r	↑ quinidine expected	Contraindicated.
	All other PIs	↑ quinidine possible	Do not coadminister.
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 CYP2D6 enzymes (e.g., atenolol, labetalol, nadolol, sotalol).
Bosentan	All PIs	With LPV/r • ↑ bosentan 48-fold (Day 4) and ↑ 5-fold (Day 10) With other PI ↑ bosentan expected With ATV (unboosted) ↓ 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, Except Diltiazem	All PIs	↑ dihydropyridine possible ↑ verapamil possible	Titrate CCB dose and monitor closely. ECG monitoring is recommended when CCB is used with ATV.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Digoxin	PI/c, PI/r	RTV 200 mg twice daily ↑ digoxin AUC 29% and ↑ half-life 43% DRV/r ↑ digoxin AUC 36% COBI ↑ digoxin C_{max} 41% and ↔ AUC	Monitor digoxin concentrations. Digoxin dose may need to be decreased. Titrate initial digoxin dose.
Diltiazem	ATV (unboosted), ATV/c, ATV/r	Unboosted ATV ↑ diltiazem AUC 125% Greater ↑ of diltiazem AUC is likely with ATV/c or ATV/r	Decrease diltiazem dose by at least 50%. If starting diltiazem, start with the lowest dose and titrate according to clinical response and adverse events. ECG monitoring is recommended.
	DRV/c, DRV/r, LPV/r	↑ diltiazem possible	Titrate diltiazem dose according to clinical response and adverse events.
Eplerenone	PI/c, PI/r	↑ eplerenone expected	Contraindicated.
Ranolazine	ATV (unboosted)	↑ ranolazine possible	Do not coadminister.
	PI/c, PI/r	↑ ranolazine expected	Contraindicated.
Ivabradine	All PIs	↑ ivabradine expected	Contraindicated.
Corticosteroids			
Beclomethasone Inhaled or intranasal	DRV/r	↔ 17-BMP (active metabolite) AUC RTV 100 mg twice daily ↑ 17-BMP AUC 2-fold	No dose adjustment needed.
	All PIs except DRV/r	↔ 17-BMP expected	No dose adjustment needed.
Budesonide, Ciclesonide, Fluticasone, Mometasone Inhaled or intranasal	All PIs	↑ glucocorticoids possible RTV 100 mg twice daily ↑ fluticasone AUC 350-fold	Do not coadminister unless the potential benefits of inhaled or intranasal corticosteroid outweigh the risks of adverse events associated with corticosteroids. Coadministration can result in adrenal insufficiency and Cushing's syndrome. Consider alternative inhaled/intranasal corticosteroid (e.g., beclomethasone).

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Betamethasone, Budesonide Systemic	All PIs	↑ glucocorticoids possible ↓ PI possible	Do not coadminister unless the potential benefits of systemic corticosteroid outweigh the risks of adverse events associated with systemic corticosteroids. Coadministration can result in adrenal insufficiency and Cushing's syndrome.
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 events associated with systemic corticosteroids. If coadministered, monitor for adrenal insufficiency, Cushing's syndrome, and other corticosteroid-related adverse events.
	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.
Glucose-Lowering Medications			
Canagliflozin	ATV (unboosted), PI/c	↔ canagliflozin	No dose adjustment needed.
	PI/r	↓ canagliflozin expected	If a patient is already tolerating canagliflozin 100 mg daily, increase canagliflozin dose to 200 mg daily. If a patient is already tolerating canagliflozin 200 mg daily and requires additional glycemic control, management strategy is based on renal function. **In Patients with eGFR ≥60 mL/min/1.73 m^2** • Canagliflozin dose may be increased to 300 mg daily. In Patients with eGFR <60 mL/min/1.73 m^2 • Consider adding another antihyperglycemic agent.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Saxagliptin	All PIs	↑ saxagliptin expected	Limit saxagliptin dose to 2.5 mg once daily.
Dapagliflozin/Saxagliptin	All PIs	↑ saxagliptin expected	Do not coadminister. Dapagliflozin is only available as a coformulated drug that contains 5 mg of saxagliptin. When coadministered with EVG/c, the dose of saxagliptin should not exceed 2.5 mg once daily; thus, this combination is not recommended.
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 needed.
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.
	ATV/c, ATV/r	No data	This HCV regimen contains RTV. If ATV is part of the ARV regimen, prescribe ATV 300 mg daily without COBI or RTV. ATV should be administered in the morning, at the same time as ombitasvir/paritaprevir/RTV plus dasabuvir. Resume RTV or COBI regimen when HCV therapy is completed.
	DRV	DRV C_{min} ↓ 43% to 48%	Do not coadminister.
	LPV/r	Paritaprevir AUC ↑ 117%	Do not coadminister.
	DRV/c	No data	Do not coadminister.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Elbasvir/Grazoprevir	ATV/r	Elbasvir AUC ↑ 4.8-fold Grazoprevir AUC ↑ 10.6-fold Elbasvir ↔ ATV Grazoprevir ↑ ATV AUC 43%	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	↑ grazoprevir expected	
Glecaprevir/Pibrentasvir	ATV (unboosted), ATV/c, ATV/r	With (ATV 300 mg plus RTV 100 mg) Once Daily • Glecaprevir AUC ↑ 6.5-fold • Pibrentasvir AUC ↑ 64%	Contraindicated.
	DRV/c, DRV/r	With (DRV 800 mg plus RTV 100 mg) Once Daily • Glecaprevir AUC ↑ 5-fold • ↔ pibrentasvir	Do not coadminister.
	LPV/r	Glecaprevir AUC ↑ 4-fold Pibrentasvir ↑ 2.5-fold	Do not coadminister.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Ledipasvir/Sofosbuvir	ATV/r	ATV AUC ↑ 33% Ledipasvir AUC ↑ 113% ↔ sofosbuvir	No dose adjustment needed. Coadministration of ledipasvir/sofosbuvir with TDF and a PI/r results in increased exposure to TDF. The safety of the increased TDF exposure has not been established. Consider alternative HCV or ARV drugs to avoid increased risk of TDF toxicities. If coadministration is necessary, monitor for TDF-related adverse events.
	ATV (unboosted), ATV/c, DRV/c, DRV/r, LPV/r	↔ PI expected ↔ ledipasvir and sofosbuvir	
Sofosbuvir/Velpatasvir	ATV/r	↔ ATV/r ↔ sofosbuvir Velpatasvir AUC ↑ 2.4-fold	No dose adjustment needed.
	DRV/r	↔ DRV/r Sofosbuvir AUC ↓ 28% ↔ velpatasvir	No dose adjustment needed.
	ATV (unboosted), ATV/c, DRV/c, LPV/r	↔ sofosbuvir and velpatasvir expected	No dose adjustment needed.
Sofosbuvir/Velpatasvir/ Voxilaprevir	ATV (unboosted), ATV/c, ATV/r	With ATV/r • Voxilaprevir AUC ↑ 4.3-fold • Velpatasvir AUC ↑ 93% • Sofosbuvir AUC ↑ 40%	Do not coadminister.
	LPV/r	↑ voxilaprevir expected	Do not coadminister.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	DRV/c, DRV/r	With DRV/r • Voxilaprevir AUC ↑ 2.4-fold • ↔ DRV/r, velpatasvir, and sofosbuvir	No dose adjustment needed.
Herbal Products			
St. John's Wort	All PIs	↓ PI expected	Contraindicated.
Hormonal Therapies			
Contraceptives—Injectable Depot MPA	LPV/r	MPA AUC ↑ 46%	No dose adjustment needed.
	All other PIs	No data	No dose adjustment needed.
Contraceptives—Oral	ATV (unboosted)	Ethinyl estradiol AUC ↑ 48% Norethindrone AUC ↑ 110%	Prescribe an oral contraceptive that contains no more than 30 mcg of ethinyl estradiol[b] or use alternative ARV or contraceptive methods. Oral contraceptives that contain less than 25 mcg of ethinyl estradiol or progestins other than norethindrone or norgestimate have not been studied.
	ATV/c	Drosperinone AUC ↑ 130% Ethinyl estradiol AUC ↓ 22%	Contraindicated with drospirenone-containing hormonal contraceptive due to potential for hyperkalemia. Use alternative ARV or contraceptive methods.
		↔ ethinyl estradiol AUC and C_{min} ↓ 25% ↔ levonorgestrel	No dose adjustment needed.
	ATV/r	Ethinyl estradiol AUC ↓ 19% and C_{min} ↓ 37% Norgestimate AUC ↑ 85% Norethindrone AUC ↑ 51% and C_{min} ↑ 67%	Oral contraceptive should contain at least 35 mcg of ethinyl estradiol.[c]
	DRV/c	Drospirenone AUC ↑ 58%	Clinical monitoring is recommended due to the potential for hyperkalemia. Use alternative ARV or contraceptive methods.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
		Ethinyl estradiol AUC ↓ 30%	
	DRV/r	Ethinyl estradiol AUC ↓ 44% and C_{min} ↓ 62% Norethindrone AUC ↓ 14% and C_{min} ↓ 30%	When Used for Contraception • Consider alternative ARV or contraceptive methods. If combined, consider using an oral contraceptive with at least 35 mcg of ethinyl estradiol. When Used for Other Clinical Indications (e.g., Acne, Menstrual Cycle Regulation) • Monitor for clinical effectiveness of hormonal therapy.
	LPV/r	Ethinyl estradiol AUC ↓ 42% and C_{min} ↓ 32% to 58% Norethindrone AUC ↓ 17% and C_{min} ↓ 32% ↔ C_{min} etonogestrel (metabolite of oral desogestrel)	Consider using an oral contraceptive with at least 35 mcg of ethinyl estradiol.
Contraceptives—Subdermal Implant Etonogestrel	LPV/r	Etonogestrel AUC ↑ 52% and C_{min} ↑ 34%	No dose adjustment needed.
	All other PIs	↑ etonogestrel expected	
Contraceptives—Subdermal Implant Levonorgestrel	All PIs	↑ levonorgestrel expected	No dose adjustment needed.
Contraceptives—Transdermal Ethinyl Estradiol/Norelgestromin	LPV/r	↔ LPV Ethinyl estradiol AUC ↓ 45% Norelgestromin AUC ↑ 83%	No dose adjustment needed.
	All other PIs	No data	

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Contraceptives—Vaginal Ring Etonogestrel/Ethinyl Estradiol	ATV/r	Ethinyl estradiol AUC ↓ 26% Etonogestrel AUC ↑ 79%	No dose adjustment needed.
	All other PIs	No data	
Contraceptives—Vaginal Ring Segesterone/Ethinyl Estradiol	All PIs	No data	Use alternative ARV or contraceptive methods.
Emergency Contraceptives Levonorgestrel (oral)	All PIs	↑ levonorgestrel expected	No dose adjustment needed.
Gender-Affirming Therapy	PI/c	↑ estradiol possible	Adjust estradiol dose as needed based on clinical effects and endogenous hormone concentrations.
	PI/r	↓ or ↑ estradiol possible	
	All PIs	↔ goserelin, leuprolide acetate, and spironolactone expected	No dose adjustment needed.
	All PIs	↑ dutasteride possible ↑ finasteride possible	Adjust dutasteride dose as needed based on clinical effects and endogenous hormone concentrations. No dose adjustment needed for finasteride.
	All PIs	↑ testosterone possible	Adjust testosterone dose as needed based on clinical effects and endogenous hormone concentrations.
Menopausal Hormone Replacement Therapy	All PIs	↓ or ↑ estrogen possible with estradiol or conjugated estrogen (equine and synthetic)	Adjust estrogen dose as needed based on clinical effects.
	All PIs	↑ drospirenone possible ↑ medroxyprogesterone ↑ micronized progesterone	Adjust progestin/progesterone dose as needed based on clinical effects. Drospirenone is not contraindicated with ATV/c products, because it is prescribed at a lower dose for menopausal HRT than products used for hormonal contraceptives.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
		See the different Contraceptives entries for other progestin-PI interactions	
Immunosuppressants			
Cyclosporine, 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 immunosuppressant-related adverse events. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with a specialist as necessary.
Everolimus	DRV/c, DRV/r	↑ immunosuppressant expected	Do not coadminister.
	All other PIs	↑ immunosuppressant expected	Initiate with an adjusted dose of immunosuppressant to account for potential increased concentrations of the immunosuppressant and monitor for immunosuppressant-related adverse events. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with a specialist as necessary.
Lipid-Modifying Agents			
Atorvastatin	ATV (unboosted), ATV/r	↑ atorvastatin possible	Administer the lowest effective atorvastatin dose while monitoring for adverse events.
	ATV/c	Atorvastatin AUC ↑ 9.2-fold and C_{max} ↑ 18.9-fold	Do not coadminister.
	DRV/c	Atorvastatin AUC ↑ 3.9-fold and C_{max} ↑ 4.2-fold	Administer the lowest effective atorvastatin dose while monitoring for adverse events. Do not exceed 20 mg atorvastatin daily.
	DRV/r	DRV/r plus atorvastatin 10 mg similar to atorvastatin 40 mg administered alone	Administer the lowest effective atorvastatin dose while monitoring for adverse events. Do not exceed 20 mg atorvastatin daily.
	LPV/r	Atorvastatin AUC ↑ 5.9-fold and C_{max} ↑ 4.7-fold	Administer the lowest effective atorvastatin dose while monitoring for adverse events. Do not exceed 20 mg atorvastatin daily.
Lomitapide	All PIs	↑ lomitapide expected	Contraindicated.
Lovastatin	All PIs	Significant ↑ lovastatin expected	Contraindicated.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Pitavastatin	All PIs	With Unboosted ATV • ↑ pitavastatin AUC 31% and C_{max} ↑ 60% • ↔ ATV With DRV/r • ↓ pitavastatin AUC 26% • ↔ DRV/r With LPV/r • ↓ pitavastatin AUC 20% • ↔ LPV	No dose adjustment needed.
Pravastatin	ATV (unboosted), ATV/c, ATV/r	No data	Administer the lowest effective pravastatin dose while monitoring for adverse events.
	DRV/c, DRV/r	With DRV/r • Pravastatin AUC ↑ 81% following single dose of pravastatin • Pravastatin AUC ↑ 23% at steady state	Administer the lowest effective pravastatin dose while monitoring for adverse events.
	LPV/r	Pravastatin AUC ↑ 33%	No dose adjustment needed.
Rosuvastatin	ATV (unboosted)	↑ rosuvastatin expected	Administer the lowest effective rosuvastatin dose while monitoring for adverse events. Do not exceed rosuvastatin 10 mg daily.
	ATV/r	Rosuvastatin AUC ↑ 3-fold and C_{max} ↑ 7-fold	
	ATV/c	Rosuvastatin AUC ↑ 3.4-fold and C_{max} ↑ 10.6-fold	
	DRV/c	Rosuvastatin AUC ↑ 1.9-fold and C_{max} ↑ 3.8-fold	Administer the lowest effective rosuvastatin dose while monitoring for adverse events. Do not exceed rosuvastatin 20 mg daily.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	DRV/r	Rosuvastatin AUC ↑ 48% and C_{max} ↑ 2.4-fold	Administer the lowest effective rosuvastatin dose while monitoring for adverse events.
	LPV/r	Rosuvastatin AUC ↑ 2.1-fold and C_{max} ↑ 4.7-fold	Administer the lowest effective rosuvastatin dose while monitoring for adverse events. Do not exceed rosuvastatin 10 mg daily.
Simvastatin	All PIs	Significant ↑ simvastatin expected	Contraindicated.
Narcotics and Treatment for Opioid Dependence			
Buprenorphine Sublingual, buccal, or implant	ATV (unboosted)	Buprenorphine AUC ↑ 93% Norbuprenorphine (active metabolite) AUC ↑ 76% ↓ ATV possible	Do not coadminister.
	ATV/r	Buprenorphine AUC ↑ 66% Norbuprenorphine (active metabolite) AUC ↑ 105%	Monitor for sedation and other signs or symptoms of overmedication. Buprenorphine dose reduction may be necessary. It may be necessary to remove implant and treat with a formulation that permits dose adjustments.
	DRV/r	↔ buprenorphine Norbuprenorphine (active metabolite) AUC ↑ 46% and C_{min} ↑ 71%	No dose adjustment needed. Monitor for buprenorphine-related adverse events. When transferring buprenorphine from transmucosal delivery to implantation, monitor to ensure buprenorphine effect is adequate and not excessive.
	LPV/r	↔ LPV/r	
	PI/c	No data	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. Monitor for buprenorphine-related adverse events.
Fentanyl	All PIs	↑ fentanyl possible	Monitor for fentanyl-related adverse events, including potentially fatal respiratory depression.
Lofexidine	ATV (unboosted)	↔ lofexidine expected	No dose adjustment needed.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	PI/c, PI/r	↑ lofexidine possible	Monitor for lofexidine-related adverse events, including symptoms of orthostasis and bradycardia.
Methadone	ATV (unboosted)	↔ ATV	No dose adjustment needed.
	PI/c	No data	Titrate methadone dose using the lowest feasible initial dose. Dose adjustment of methadone may be needed. Monitor for methadone-related adverse events.
	All PI/r	ATV/r and DRV/r ↓ R-methadone[d] AUC 16% to 18% LPV/r ↓ methadone AUC 26% to 53%	Opioid withdrawal is unlikely but may occur. Monitor for opioid withdrawal and increase methadone dose as clinically indicated.
Oxycodone	All PIs	LPV/r ↑ oxycodone AUC 2.6-fold Other PIs: ↑ oxycodone expected	Monitor for opioid-related adverse events, including potentially fatal respiratory depression. Oxycodone dose reduction may be necessary.
Tramadol	All PIs	↑ tramadol expected ↓ M1 (active metabolite) possible	Tramadol dose adjustments may be necessary. Monitor for clinical response and tramadol-related adverse events.
PDE5 Inhibitors			
Avanafil	ATV (unboosted)	No data	Avanafil dose should not exceed 50 mg once every 24 hours.
	PI/c, PI/r	RTV 600 mg twice daily (for 5 days) ↑ avanafil AUC 13-fold and ↑ C_{max} 2.4-fold	Do not coadminister.
Sildenafil	All PIs	DRV/r plus sildenafil 25 mg similar to sildenafil 100 mg alone RTV 500 mg twice daily ↑ sildenafil AUC 1,000%	For Treatment of Erectile Dysfunction • Start with sildenafil 25 mg every 48 hours and monitor for adverse events of sildenafil. Contraindicated for treatment of PAH.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Tadalafil	All PIs	RTV 200 mg twice daily ↑ tadalafil AUC 124%	For Treatment of Erectile Dysfunction • Start with tadalafil 5 mg and do not exceed a single dose of tadalafil 10 mg every 72 hours. Monitor for adverse events 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 twice daily ↑ vardenafil AUC 49-fold	Start with vardenafil 2.5 mg every 72 hours and monitor for adverse events of vardenafil.
Sedative/Hypnotics			
Alprazolam, Clonazepam, Diazepam	All PIs	↑ benzodiazepine possible RTV 200 mg twice daily (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 and, therefore, have less interaction potential than other benzodiazepines.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Midazolam	All PIs	↑ midazolam expected	Oral midazolam is contraindicated with PIs. Parenteral midazolam can be used with caution when given in a monitored situation with appropriate medical management available in case of respiratory sedation and/or prolonged sedation. Consider dose reduction, especially if more than a single dose of midazolam is administered.
Suvorexant	All PIs	↑ suvorexant expected	Do not coadminister.
Triazolam	All PIs	↑ triazolam expected RTV 200 mg twice daily ↑ triazolam half-life 1,200% and ↑ AUC 2,000%	Contraindicated.
Zolpidem	PI/c, PI/r	↑ zolpidem possible	Initiate zolpidem at a low dose and monitor for zolpidem-related adverse events. 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 twice daily ↑ 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 • If original dose was colchicine 0.6 mg twice daily, decrease to colchicine 0.3 mg once daily. If dose was 0.6 mg once daily, decrease to 0.3 mg every other day. For Treatment of Familial Mediterranean Fever • Do not exceed colchicine 0.6 mg once daily or colchicine 0.3 mg twice daily. Contraindicated in patients with hepatic (Child-Pugh Score A, B, or C) or renal impairment (CrCl <60 mL/min).

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Dronabinol	All PIs	↑ dronabinol possible	Monitor for dronabinol-related adverse events.
Eluxadoline	All PIs	↑ eluxadoline expected	Administer eluxadoline at a dose of 75 mg twice daily and monitor for eluxadoline-related adverse events.
Ergot Derivatives	All PIs	↑ dihydroergotamine, ergotamine, and methylergonovine expected	Contraindicated.
Flibanserin	All PIs	↑ flibanserin expected	Contraindicated.

[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: Lo Minastrin Fe; Lo Loestrin Fe; Loestrin 1/20, 1.5/30; Loestrin Fe 1/20, 1.5/30; Loestrin 24 Fe; Minastrin 24 Fe; Ortho Tri-Cyclen Lo. Generic formulations also may be available.

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

[d] R-methadone is the active form of methadone.

Key to Symbols

↑ = increase
↓ = decrease
↔ = no change

Key: 17-BMP = beclomethasone 17-monopropionate; ALT = alanine aminotransferase; ART = antiretroviral therapy; ARV = antiretroviral; AST = aspartate aminotransferase; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; C_{max} = maximum plasma concentration; C_{min} = minimum plasma concentration; CCB = calcium channel blocker; 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; EVG/c = elvitegravir/cobicistat; GI = gastrointestinal; H2RA = H2 receptor antagonist; HCV = hepatitis C virus; HRT = hormone replacement therapy; INR = international normalized ratio; LPV = lopinavir; LPV/r = lopinavir/ritonavir; MPA = medroxyprogesterone acetate; 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; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant; TDF = tenofovir disoproxil fumarate; VPA = valproic acid

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

This table provides information on the known or predicted interactions between non-nucleoside reverse transcriptase inhibitors (NNRTIs) and non-antiretroviral (ARV) drugs. Cabotegravir (CAB) intramuscular (IM) plus rilpivirine (RPV) IM are co-packaged into a single product and are coadministered as a complete regimen; therefore, the dosing recommendations and clinical comments reflect the combination of CAB IM and RPV IM treatments. Drug interaction studies were not conducted with either CAB IM or RPV IM. Drug interaction studies with oral CAB and RPV were leveraged to make the dosing recommendations for CAB IM and RPV IM. For information regarding interactions between NNRTIs and other ARV drugs, including dosing recommendations, refer to Tables 24c, 24e, 24f, 25a, and 25b.

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. When an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgment to select the most appropriate alternative medication to use.

RPV 75 mg and 300 mg oral once daily (3 and 12 times the recommended dose, respectively) were shown to prolong the QTc interval. Known and expected/theoretical pharmacokinetic interactions, resulting in increased RPV exposures, are included in this table due to the safety concern of QTc prolongation. There is limited information about the potential for pharmacodynamic interactions between RPV (in the absence of increased RPV exposures) and drugs that prolong the QTc interval; therefore, these are not included in this table.

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers			
Antacids	DOR, EFV, NVP	↔ NNRTI AUC	No dose adjustment needed.
	ETR	↔ ETR expected	No dose adjustment needed.
	RPV IM	↔ RPV expected	No dose adjustment needed.
	RPV PO	↓ RPV expected when given simultaneously	Give antacids at least 2 hours before or at least 4 hours after RPV.
H2 Receptor Antagonists	DOR, NVP	↔ NNRTI expected	No dose adjustment needed.
	EFV	↔ EFV AUC	No dose adjustment needed.
	ETR	↔ ETR AUC	No dose adjustment needed.
	RPV IM	↔ RPV expected	No dose adjustment needed.
	RPV PO	RPV AUC ↓ 76% when famotidine 40 mg is taken 2 hours prior	Give H2 receptor antagonists at least 12 hours before or at least 4 hours after RPV.
Proton Pump Inhibitors	DOR	DOR AUC ↓ 17% and C_{min} ↓ 16%	No dose adjustment needed.
	EFV, NVP	↔ EFV and NVP expected	
	ETR	With Omeprazole 40 mg Daily ETR AUC ↑ 41%	

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	RPV IM	↔ RPV expected	No dose adjustment needed.
	RPV PO	With Omeprazole 20 mg Daily RPV AUC ↓ 40% and C_{min} ↓ 33%	Contraindicated.
Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia			
Alfuzosin,Doxazosin, Silodosin, Terazosin	DOR, RPV IM, RPV PO	↔ alpha-adrenergic antagonists expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ alpha-adrenergic antagonists expected	Consider alternative ARV or alpha-antagonist therapy. If coadministration is necessary, monitor for therapeutic effectiveness of alpha antagonist.
Tamsulosin	DOR, RPV IM, RPV PO	↔ tamsulosin expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ tamsulosin expected	Monitor for therapeutic effectiveness of tamsulosin after 2–4 weeks. May need to increase dose to tamsulosin 0.8 mg once daily for patients who fail to respond to the 0.4-mg dose.
Antimycobacterials			
Bedaquiline	DOR, RPV IM, RPV PO	↔ bedaquiline expected	No dose adjustment needed.
	EFV, ETR	↓ bedaquiline possible	Do not coadminister.
	NVP	↔ bedaquiline AUC	No dose adjustment needed.
Rifabutin	DOR	DOR AUC ↓ 50%	Increase DOR dose to 100 mg twice daily. No dose adjustment is needed for rifabutin.
	EFV	Rifabutin ↓ 38%	The recommended dosing range is rifabutin 450–600 mg per day.
	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.
	NVP	Rifabutin AUC ↑ 17% and metabolite AUC ↑ 24% NVP C_{min} ↓ 16%	No dose adjustment needed.
	RPV IM	↓ RPV expected	Contraindicated.
	RPV PO	Rifabutin plus RPV 50 mg PO Once Daily Compared to RPV 25 mg Once Daily Alone ↔ RPV AUC and C_{min}	Increase RPV dose to 50 mg PO once daily. No dose adjustment for rifabutin is needed.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Rifampin	DOR	DOR AUC ↓ 88%	**Contraindicated.** After stopping rifampin, wait 4 weeks before initiating DOR.
	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 IM	↓ RPV expected	**Contraindicated.**
	RPV PO	RPV AUC ↓ 80%	**Contraindicated.**
Rifapentine	DOR	**DOR 100 mg Twice Daily plus Once-Weekly Rifapentine and Isoniazid Compared to DOR 100 mg Twice Daily Alone** DOR AUC ↓ 29%, C_{min} ↓ 31%	**Contraindicated.** After stopping rifapentine, wait 4 weeks before initiating DOR.
	EFV	↔ EFV concentrations	No dose adjustment needed.
	ETR	↓ ETR possible	**Do not coadminister.**
	NVP	NVP C_{min} ↓ 27%	**Do not coadminister.**
	RPV IM, RPV PO	↓ RPV expected	**Contraindicated.**
Antibacterials—Macrolides			
Azithromycin	All NNRTIs	↔ azithromycin expected	No dose adjustment needed.
Clarithromycin	DOR	↔ clarithromycin expected ↑ DOR possible	Monitor for ARV tolerability if used in combination.
	EFV	Clarithromycin AUC ↓ 39%	Monitor for effectiveness, or consider alternative agent (e.g., azithromycin) for MAC prophylaxis and treatment.
	ETR	Clarithromycin AUC ↓ 39% ETR AUC ↑ 42%	Consider alternative macrolide (e.g., azithromycin) for MAC prophylaxis and treatment.
	NVP	Clarithromycin AUC ↓ 31% NVP AUC ↑ 26%	Monitor for effectiveness, or consider alternative macrolide (e.g., azithromycin) for MAC prophylaxis and treatment.
	RPV IM, RPV PO	↔ clarithromycin expected ↑ RPV possible	Consider alternative macrolide (e.g., azithromycin) for MAC prophylaxis and treatment. If coadministered, monitor for QTc prolongation.
Erythromycin	DOR	↑ DOR possible	Monitor for ARV tolerability if used in combination.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	EFV, ETR, NVP	↑ EFV, ETR, and NVP possible ↓ erythromycin possible	Monitor for ARV tolerability and antibiotic efficacy if used in combination.
	RPV IM, RPV PO	↑ RPV possible	Consider alternative macrolide (e.g., azithromycin). If coadministered, monitor for QTc prolongation.
Anticoagulants			
Apixaban	DOR, RPV IM, RPV PO	↔ apixaban expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ apixaban possible	Consider alternative ARV or anticoagulant therapy.
Dabigatran	All NNRTIs	↔ dabigatran expected	No dose adjustment needed.
Edoxaban	All NNRTIs	↔ edoxaban expected	No dose adjustment needed.
Rivaroxaban	DOR, RPV IM, RPV PO	↔ rivaroxaban expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ rivaroxaban possible	Consider alternative ARV or anticoagulant therapy.
Warfarin	DOR, RPV IM, RPV PO	↔ warfarin expected	No dose adjustment needed.
	EFV, ETR, NVP	↑ or ↓ warfarin possible	Monitor INR and adjust warfarin dose accordingly.
Anticonvulsants			
Carbamazepine, Phenobarbital, Phenytoin	DOR	↓ DOR possible	Contraindicated. After stopping anticonvulsant, wait 4 weeks before initiating DOR.
	EFV	Carbamazepine plus EFV Carbamazepine AUC ↓ 27% EFV AUC ↓ 36% Phenytoin plus EFV ↓ EFV ↑ or ↓ phenytoin possible	Consider alternative ARV or anticonvulsant. If coadministration is necessary, monitor anticonvulsant and EFV concentrations.
	ETR	↓ anticonvulsant and ETR possible	Do not coadminister.
	NVP	↓ anticonvulsant and NVP possible	Consider alternative ARV or anticonvulsant. If coadministration is necessary, monitor anticonvulsant and NVP concentrations and virologic response.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	RPV IM, RPV PO	↓ RPV possible	Contraindicated.
Eslicarbazepine	All NNRTIs	↓ NNRTI possible	Consider alternative ARV or anticonvulsant. If coadministration is necessary, monitor virologic response and consider monitoring plasma concentrations of ARVs.
Oxcarbazepine	DOR, RPV IM, RPV PO	↓ NNRTI possible	Contraindicated.
	EFV, ETR, NVP	↓ NNRTI possible	Consider alternative ARV or anticonvulsant. If coadministration is necessary, monitor virologic response and consider monitoring plasma concentrations of ARVs.
Ethosuximide, Lacosamide, Tiagabine, Zonisamide	DOR, RPV IM, RPV PO	↔ anticonvulsant expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ anticonvulsant possible	Monitor seizure control. Consider anticonvulsant therapeutic drug monitoring.
Lamotrigine	DOR, ETR, NVP, RPV IM, RPV PO	↔ lamotrigine expected	No dose adjustment needed.
	EFV	↓ lamotrigine possible	Monitor seizure control and plasma concentrations of lamotrigine.
Antidepressants, Anxiolytics, and Antipsychotics Also see the Sedative/Hypnotics section below.			
Bupropion	DOR, ETR, RPV IM, RPV PO	↔ bupropion expected	No dose adjustment needed.
	EFV	Bupropion AUC ↓ 55%	Titrate bupropion dose based on clinical response.
	NVP	↓ bupropion possible	
Citalopram, Escitalopram	DOR, RPV IM, RPV PO	↔ antidepressant expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ antidepressant possible	Titrate antidepressant dose based on clinical response.
Fluoxetine, Fluvoxamine	All NNRTIs	↔ antidepressant expected	No dose adjustment needed.
Paroxetine	DOR, NVP, RPV IM, RPV PO	↔ paroxetine expected	No dose adjustment needed.
	EFV, ETR	↔ paroxetine expected	No dose adjustment needed.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Nefazodone	DOR, RPV IM, RPV PO	↑ NNRTI possible	No dose adjustment needed.
	EFV, ETR, NVP	↓ nefazodone expected ↑ NNRTI possible	Monitor antidepressant effect. Titrate dose as necessary based on clinical response.
Sertraline	DOR, RPV IM, RPV PO	↔ sertraline expected	No dose adjustment needed.
	EFV	Sertraline AUC ↓ 39%	Monitor the antidepressant effect. Titrate dose as necessary based on clinical response.
	ETR, NVP	↓ sertraline possible	
Trazodone	DOR, RPV IM, RPV PO	↔ trazodone expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ trazodone possible	Monitor for therapeutic effectiveness of trazodone and titrate dose as necessary.
Antipsychotics			
Aripiprazole	DOR, RPV IM, RPV PO	↔ aripiprazole expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ aripiprazole expected	Monitor for therapeutic effectiveness of antipsychotic. Consider doubling usual dose of aripiprazole over 1–2 weeks. Refer to aripiprazole prescribing information for dose recommendations.
Brexpiprazole	DOR, RPV IM, RPV PO	↔ brexpiprazole expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ brexpiprazole expected	Monitor for therapeutic effectiveness of antipsychotic. Consider doubling the usual dose of brexpiprazole and making further adjustments based on clinical response. Refer to brexpiprazole prescribing information.
Cariprazine	DOR, RPV IM, RPV PO	↔ cariprazine expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ cariprazine and ↑ or ↓ active metabolite possible	Do not coadminister.
Iloperidone	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	EFV, ETR, NVP	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.
Lumateperone	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ antipsychotic possible	Do not coadminister.
Lurasidone	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.
Olanzapine	DOR, ETR, NVP, RPV IM, RPV PO	↔ olanzapine expected	No dose adjustment needed.
	EFV	↓ olanzapine possible	Monitor for therapeutic effectiveness of olanzapine.
Other Antipsychotics CYP3A4 substrates (e.g., clozapine, perphenazine, risperidone)	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.
Pimavanserin	DOR, RPV IM, RPV PO	↔ pimavanserin expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ pimavanserin expected	Do not coadminister.
Pimozide	DOR, RPV IM, RPV PO	↔ pimozide expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ pimozide possible	Monitor for therapeutic effectiveness of pimozide.
Quetiapine	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.
Ziprasidone	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antifungals			
Fluconazole	DOR	↑ DOR possible	No dose adjustment needed.
	EFV	↔ fluconazole expected ↔ EFV AUC	No dose adjustment needed.
	ETR	ETR AUC ↑ 86%	No dose adjustment needed.
	NVP	NVP AUC ↑ 110%	Consider alternative ARV or antifungal agent. Increased risk of hepatotoxicity is possible with this combination.
	RPV IM, RPV PO	↑ RPV possible	No dose adjustment needed. If coadministered, consider monitoring for QTc prolongation.
Isavuconazole	DOR	↑ DOR possible	No dose adjustment needed.
	EFV, ETR, NVP	↓ isavuconazole possible	Monitor isavuconazole concentration and antifungal response. Dose adjustments for isavuconazole may be necessary.
	RPV IM, RPV PO	↑ RPV possible	No dose adjustment needed. If coadministered, consider monitoring for QTc prolongation.
Itraconazole	DOR	↑ DOR possible	No dose adjustment needed.
	EFV	Itraconazole and OH-itraconazole AUC, C_{max}, and C_{min} ↓ 37% to 44%	Do not coadminister unless potential benefits outweigh the risks. Failure to achieve therapeutic itraconazole concentrations has been reported. If coadministration is necessary, closely monitor itraconazole concentration and adjust dose accordingly.
	ETR	↓ itraconazole possible ↑ ETR possible	Dose adjustments for itraconazole may be necessary. Monitor itraconazole concentration and antifungal response.
	NVP	Itraconazole AUC ↓ 61% ↑ NVP possible	Do not coadminister unless potential benefits outweigh the risks. If coadministration is necessary, monitor itraconazole concentration and adjust dose accordingly.
	RPV IM, RPV PO	↑ RPV possible	No dose adjustment needed. If coadministered, consider monitoring for QTc prolongation.
Posaconazole	DOR, ETR, NVP	↑ NNRTI possible	No dose adjustment needed.
	EFV	Posaconazole AUC ↓ 50% ↔ EFV AUC	Do not coadminister unless potential benefits outweigh the risks. If coadministration is necessary, monitor posaconazole concentration and adjust dose accordingly.
	RPV IM, RPV PO	↑ RPV possible	No dose adjustment needed. If coadministered, consider monitoring for QTc prolongation.
	DOR	↑ DOR possible	No dose adjustment needed.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Voriconazole	EFV	Voriconazole AUC ↓ 77% EFV AUC ↑ 44%	Contraindicated at standard doses. Adjust dose to voriconazole 400 mg twice daily plus EFV 300 mg daily.
	ETR	↔ voriconazole AUC ETR AUC ↑ 36%	No dose adjustment needed.
	NVP	↓ voriconazole possible ↑ NVP possible	Consider alternative ARV or antifungal agent. If coadministration is necessary, monitor ARV tolerability and antifungal response and/or voriconazole concentration.
	RPV IM, RPV PO	↑ RPV possible	No dose adjustment needed. If coadministered, consider monitoring for QTc prolongation.
Antimalarials			
Artemether/Lumefantrine	DOR, RPV IM, RPV PO	↔ antimalarial expected	No dose adjustment needed.
	EFV	Artemether AUC ↓ 79% DHA AUC ↓ 75% Lumefantrine AUC ↓ 30% to 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 is 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 two studies, but ↑ 50% to 56% in another.	Clinical significance is unknown. If used in combination, monitor closely for antimalarial efficacy and lumefantrine toxicity.
Atovaquone/Proguanil	DOR, ETR, NVP, RPV IM, RPV PO	No data	Monitor for antimalarial efficacy.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	EFV	Atovaquone AUC ↓ 75% Proguanil AUC ↓ 43%	No dose recommendation. Consider alternative drug for malaria prophylaxis, if possible.
Antiplatelets			
Clopidogrel	DOR, NVP, RPV IM, RPV PO	↔ clopidogrel expected	No dose adjustment needed.
	EFV, ETR	↓ activation of clopidogrel possible	Consider alternative ARV or antiplatelet. ETR may prevent metabolism of clopidogrel to its active metabolite.
Prasugrel	All NNRTIs	↔ prasugrel expected	No dose adjustment needed.
Ticagrelor	DOR, RPV IM, RPV PO	↔ ticagrelor expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ ticagrelor expected	Consider alternative ARV or anticoagulant therapy.
Vorapaxar	DOR, NVP, RPV IM, RPV PO	↔ vorapaxar expected	No dose adjustment needed.
	EFV, ETR	↓ vorapaxar expected	Insufficient data to make a dose recommendation.
Antipneumocystis and Anti-Toxoplasmosis Drugs			
Atovaquone (oral solution)	DOR, ETR, NVP, RPV IM, RPV PO	No data	Monitor for therapeutic effectiveness of atovaquone.
	EFV	Atovaquone AUC ↓ 44% to 47%	Consider alternative ARV or agent for PCP or toxoplasmosis treatment or prophylaxis. If coadministration is necessary, monitor for therapeutic effectiveness of atovaquone.
Antivirals—Orthopoxviruses (Smallpox, Mpox)			
Brincidofovir	All NNRTIs	↔ brincidofovir expected	No dose adjustment needed.
Cidofovir	All NNRTIs	↔ cidofovir expected	No dose adjustment needed.
Tecovirimat	DOR, RPV PO	↓ DOR or RPV expected but not likely to be clinically relevant	No dose adjustment needed.
	EFV, ETR, NVP	↔ EFV, ETR, or NVP expected	No dose adjustment needed.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	RPV IM	↓ RPV expected but not likely to be clinically relevant	No dose adjustment needed. If there is a concern for suboptimal RPV exposure, seek expert consultation. Do not initiate CAB/RPV IM during and within 2 weeks after tecovirimat treatment. (Refer to Table 24d for interaction with CAB.)
Cardiac Medications			
Bosentan	DOR	↓ DOR possible	Consider alternative ARV or alternative to bosentan. If coadministration is necessary, monitor virologic response.
	EFV, ETR, NVP	↓ NNRTI possible ↓ bosentan possible	Consider alternative ARV or alternative to bosentan. If coadministration is necessary, monitor bosentan efficacy and virologic response.
	RPV IM, RPV PO	↓ RPV possible	Consider alternative ARV or alternative to bosentan. If coadministration is necessary, monitor virologic response.
Dihydropyridine CCBs	DOR, RPV IM, RPV PO	↔ CCBs expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ CCBs possible	Titrate CCB dose based on clinical response.
Diltiazem, Verapamil	DOR, RPV IM, RPV PO	↔ CCBs expected ↑ NNRTI possible	No dose adjustment needed.
	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 IM, RPV PO	Significant ↓ RPV possible	Contraindicated with more than a single dose of dexamethasone.
Glucose-Lowering Agents			
Canagliflozin, Dapagliflozin, Empagliflozin, Sitagliptin	All NNRTIs	↔ antihyperglycemic expected	No dose adjustment needed.
Linagliptin, Saxagliptin	DOR, RPV IM, RPV PO	↔ antihyperglycemic expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ antihyperglycemic possible	Monitor glycemic control.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Metformin	DOR	↔ metformin AUC DOR AUC ↓ 26% and C_{max} ↓ 24%	No dose adjustment needed.
	EFV, ETR, NVP	↔ metformin expected	No dose adjustment needed.
	RPV IM	↔ metformin expected	No dose adjustment needed.
	RPV PO	↔ metformin AUC	No dose adjustment needed.
Hepatitis C Direct-Acting Antiviral Agents			
Daclatasvir	DOR, RPV IM, RPV PO	No data	No dose adjustment needed.
	EFV, ETR, NVP	Daclatasvir 120 mg Once Daily plus EFV 600 mg Daily Compared to Daclatasvir 60 mg Alone Daclatasvir C_{min} ↓ 17% and AUC ↑ 37%	The recommended dose is daclatasvir 90 mg once daily.
Dasabuvir plus Paritaprevir/ Ombitasvir/RTV	DOR	↑ DOR possible	No dose adjustment needed.
	EFV	No data	Contraindicated.
	ETR, NVP	↓ DAAs possible	Do not coadminister.
	RPV IM	↑ RPV expected	Do not coadminister due to the potential for QTc prolongation with higher concentrations of RPV.
	RPV PO	RPV AUC ↑ 150% to 225%	Do not coadminister due to the potential for QTc prolongation with higher concentrations of RPV.
Elbasvir/Grazoprevir	DOR	↔ elbasvir and grazoprevir DOR AUC ↑ 56% and C_{min} ↑ 41%	No dose adjustment needed.
	EFV	Elbasvir AUC ↓ 54% Grazoprevir AUC ↓ 83% ↔ EFV	Contraindicated.
	ETR, NVP	↓ elbasvir and grazoprevir expected	Do not coadminister.
	RPV IM	↔ elbasvir and grazoprevir expected ↔ RPV expected	No dose adjustment needed.
	RPV PO	↔ elbasvir and grazoprevir ↔ RPV AUC and C_{min}	No dose adjustment needed.
Glecaprevir/Pibrentasvir	DOR	↑ DOR expected	No dose adjustment needed.
	EFV	↓ glecaprevir and pibrentasvir expected	Do not coadminister.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	ETR	↓ glecaprevir and pibrentasvir possible	Do not coadminister.
	NVP	↓ glecaprevir and pibrentasvir possible	Consider alternative ARV or HCV regimen. If coadministration is necessary, monitor for HCV treatment efficacy.
	RPV IM	↔ glecaprevir and pibrentasvir expected ↑ RPV expected	No dose adjustment needed.
	RPV PO	↔ glecaprevir and pibrentasvir RPV AUC ↑ 84%	No dose adjustment needed.
Ledipasvir/Sofosbuvir	DOR	↔ ledipasvir and sofosbuvir ↔ DOR	No dose adjustment needed.
	EFV	Ledipasvir AUC, C_{min}, and C_{max} ↓ 34% ↔ sofosbuvir	
	ETR, NVP	No significant effect expected	
	RPV IM	↔ ledipasvir, sofosbuvir, and RPV expected	
	RPV PO	↔ ledipasvir and sofosbuvir ↔ RPV	
Sofosbuvir/Velpatasvir	DOR, RPV IM, RPV PO	No significant effect expected	No dose adjustment needed.
	EFV	Velpatasvir AUC ↓ 43%, C_{max} ↓ 37%, and C_{min} ↓ 47%	Do not coadminister.
	ETR, NVP	↓ velpatasvir expected	Do not coadminister.
Sofosbuvir/Velpatasvir/ Voxilaprevir	DOR, RPV IM, RPV PO	No significant effect expected	No dose adjustment needed.
	EFV	Velpatasvir AUC ↓ 43%, C_{max} ↓ 37%, and C_{min} ↓47% ↓ voxilaprevir expected	Do not coadminister.
	ETR, NVP	↓ voxilaprevir expected ↓ velpatasvir expected	Do not coadminister.
Herbal Products			
St. John's Wort	DOR	↓ DOR expected	Contraindicated. After stopping St. John's Wort, wait 4 weeks before initiating DOR.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	EFV, ETR, NVP	↓ EFV, ETR, and NVP expected	Do not coadminister.
	RPV IM, RPV PO	↓ RPV expected	Contraindicated.
Hormonal Therapies			
Contraceptives—Injectable Depot MPA	DOR, ETR, RPV IM, RPV PO	↔ MPA expected	No dose adjustment needed.
	EFV, NVP	↔ MPA	No dose adjustment needed.
Contraceptives—Oral	DOR	↔ ethinyl estradiol ↔ levonorgestrel	No dose adjustment needed.
	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%	When Used for Contraception Use alternative ARV or contraceptive methods. When Used for Other Clinical Indications (e.g., Acne, Menstrual Cycle Regulation) Monitor for clinical effectiveness of hormonal therapy.
	ETR	Ethinyl estradiol AUC ↑ 22% ↔ norethindrone	No dose adjustment needed.
	NVP	Ethinyl estradiol AUC ↓ 29% and C_{min} ↓ 58% Norethindrone AUC ↓ 18% Etonogestrel (metabolite of oral desogestrel) C_{min} ↓ 22%	No dose adjustment needed based on clinical data that demonstrated no change in effectiveness.
	RPV IM	↔ ethinyl estradiol expected ↔ norethindrone expected	No dose adjustment needed.
	RPV PO	↔ ethinyl estradiol ↔ norethindrone	No dose adjustment needed.
Contraceptives—Subdermal Implant Etonogestrel	DOR, RPV IM, RPV PO	↔ etonogestrel expected	No dose adjustment needed.
	EFV	Etonogestrel AUC ↓ 63% to 82%	Use alternative ARV or contraceptive methods.
	ETR	↓ etonogestrel possible	No data available to make dose recommendation.
	NVP	↔ etonogestrel	No dose adjustment needed.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Contraceptives—Subdermal Implant Levonorgestrel	DOR, RPV IM, RPV PO	↔ levonorgestrel expected	No dose adjustment needed.
	EFV	Levonorgestrel AUC ↓ 42% to 47%	Use alternative ARV or contraceptive methods. Unintended pregnancies were observed in women who used EFV and levonorgestrel implant concomitantly.
	ETR	↓ levonorgestrel possible	No data available to make dose recommendation.
	NVP	Levonorgestrel AUC ↑ 35%	No dose adjustment needed.
Contraceptives—Transdermal Ethinyl Estradiol/ Norelgestromin	DOR, RPV IM, RPV PO	↔ ethinyl estradiol or norelgestromin expected	No dose adjustment needed.
	EFV	↓ ethinyl estradiol or norelgestromin expected	No data available to make dose recommendation.
	ETR, NVP	↓ ethinyl estradiol or norelgestromin possible	No data available to make dose recommendation.
Contraceptives—Vaginal Ring Etonogestrel/Ethinyl Estradiol	DOR, RPV IM, RPV PO	↔ etonogestrel and ethinyl estradiol expected	No dose adjustment needed.
	EFV	Ethinyl estradiol (intravaginal ring) AUC ↓ 56% Etonogestrel (intravaginal ring) AUC ↓ 81%	Consider alternative ARV or contraceptive method.
	ETR, NVP	↓ etonogestrel and ethinyl estradiol possible	No data available to make dose recommendation.
Contraceptives—Vaginal Ring Segesterone/Ethinyl Estradiol	DOR, RPV IM, RPV PO	↔ segesterone and ethinyl estradiol expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ segesterone and ethinyl estradiol possible	No data available to make dose recommendation.
Emergency Contraceptives Levonorgestrel (oral)	DOR, RPV IM, RPV PO	↔ levonorgestrel expected	No dose adjustment needed.
	EFV	Levonorgestrel AUC ↓ 58%	Effectiveness of emergency postcoital contraception may be diminished.
	NVP, ETR	↓ levonorgestrel possible	No data available to make dose recommendation.
Gender-Affirming Therapy	DOR, RPV IM, RPV PO	↔ hormonal concentrations expected	No dose adjustment needed.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	EFV, ETR, NVP	↓ estradiol possible ↓ cyproterone and progestogens possible ↔ goserelin, leuprolide acetate, and spironolactone expected ↓ dutasteride and finasteride possible	Monitor feminizing effects of estrogen and antiandrogen therapy. Titrate dose as necessary to achieve therapeutic goals.
	EFV, ETR, NVP	↓ testosterone possible	Monitor masculinizing effects of testosterone. Titrate testosterone dose as necessary to achieve therapeutic goals.
Menopausal Replacement Therapy	DOR, RPV IM, RPV PO	↔ hormonal concentrations expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ estrogen possible with estradiol or conjugated estrogen (equine and synthetic) ↓ medroxyprogesterone possible ↓ micronized progesterone possible ↓ drospirenone possible See Contraceptives—Oral above for other progestin-NNRTI interactions	Monitor menopausal symptoms. Titrate to the dose of hormonal therapy that achieves menopausal symptom relief.
Immunosuppressants			
Cyclosporine	DOR, RPV IM, RPV PO	↔ cyclosporine expected ↑ NNRTI possible	No dose adjustment needed.
	EFV, ETR, NVP	↓ cyclosporine possible	Increase in immunosuppressant dose may be necessary. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with specialist as necessary.
Everolimus, Sirolimus, Tacrolimus	DOR, RPV IM, RPV PO	↔ immunosuppressant expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ immunosuppressant possible	Increase in immunosuppressant dose may be necessary. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with specialist as necessary.
Lipid-Modifying Agents			
	DOR	↔ atorvastatin AUC	No dose adjustment needed.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
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.
	RPV IM	↔ atorvastatin expected	No dose adjustment needed.
	RPV PO	↔ atorvastatin AUC	No dose adjustment needed.
Fluvastatin	DOR, NVP, RPV IM, RPV PO	↔ fluvastatin expected	No dose adjustment needed.
	EFV, ETR	↑ fluvastatin possible	Dose adjustments for fluvastatin may be necessary. Monitor for fluvastatin toxicity.
Lovastatin, Simvastatin	DOR, RPV IM, RPV PO	↔ lovastatin and simvastatin expected	No dose adjustment needed.
	EFV	Simvastatin AUC ↓ 60% to 68% Simvastatin active metabolite AUC ↓ 60%	Adjust simvastatin dose according to lipid response, but do not exceed the maximum recommended dose.
	ETR, NVP	↓ lovastatin possible ↓ simvastatin possible	Adjust lovastatin or simvastatin dose according to lipid response, but do not exceed the maximum recommended dose.
Pitavastatin	DOR, ETR, NVP, RPV IM, RPV PO	↔ pitavastatin expected	No dose adjustment needed.
	EFV	↔ pitavastatin AUC	No dose adjustment needed.
Pravastatin	DOR, NVP, RPV IM, RPV PO	↔ pravastatin expected	No dose adjustment needed.
	EFV	Pravastatin AUC ↓ 44%	Adjust statin dose according to lipid responses, but do not exceed the maximum recommended dose.
	ETR	↓ pravastatin possible	
Rosuvastatin	DOR, EFV, ETR, NVP, RPV IM, RPV PO	↔ rosuvastatin expected	No dose adjustment needed.
Narcotics and Treatment for Opioid Dependence			
Buprenorphine	DOR, RPV IM, RPV PO	↔ buprenorphine expected	No dose adjustment needed.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Sublingual or buccal	EFV	Buprenorphine AUC ↓ 50% Norbuprenorphine (active metabolite) AUC ↓ 71%	No dose adjustment needed, monitor for withdrawal symptoms.
	ETR	Buprenorphine AUC ↓ 25%	No dose adjustment needed.
	NVP	No significant effect	No dose adjustment needed.
Buprenorphine Implant	DOR, RPV IM, RPV PO	↔ buprenorphine expected	No dose adjustment needed.
	EFV, ETR, NVP	No data	Clinical monitoring is recommended when NNRTI is initiated after insertion of buprenorphine implant.
Lofexidine	DOR, EFV, ETR, NVP, RPV IM, RPV PO	↔ lofexidine expected	No dose adjustment needed.
Methadone	DOR	↔ methadone AUC DOR AUC ↓ 26%	No dose adjustment needed.
	EFV	Methadone AUC ↓ 52%	Opioid withdrawal common; monitor and increase methadone dose as necessary.
	ETR	↔ methadone AUC	No dose adjustment needed.
	NVP	Methadone AUC ↓ 37% to 51% ↔ NVP	Opioid withdrawal common; monitor and increase methadone dose as necessary.
	RPV IM	↓ methadone AUC expected	No dose adjustment needed, but monitor for withdrawal symptoms.
	RPV PO	R-methadone[a] AUC ↓ 16%	No dose adjustment needed, but monitor for withdrawal symptoms.
PDE5 Inhibitors			
Sildenafil	DOR	↔ sildenafil expected	No dose adjustment needed.
	EFV, NVP	↓ sildenafil possible	May need to titrate sildenafil dose based on clinical effect.
	ETR	Sildenafil AUC ↓ 57%	May need to titrate sildenafil dose based on clinical effect.
	RPV IM	↔ sildenafil expected	No dose adjustment needed.
	RPV PO	↔ sildenafil AUC and C_{max}	No dose adjustment needed.
Tadalafil	DOR, RPV IM, RPV PO	↔ tadalafil expected	No dose adjustment needed.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	EFV, ETR, NVP	↓ tadalafil possible	May need to titrate tadalafil dose based on clinical effect.
Avanafil, Vardenafil	DOR, RPV IM, RPV PO	↔ avanafil or vardenafil expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ avanafil or vardenafil possible	May need to increase PDE5 inhibitor dose based on clinical effect.
Sedative/Hypnotics			
Alprazolam, Triazolam	DOR, RPV IM, RPV PO	↔ alprazolam or triazolam expected	No dose adjustment needed.
	EFV, ETR, NVP	↓ alprazolam or triazolam possible	Monitor for therapeutic effectiveness of benzodiazepine.
Diazepam	DOR, RPV IM, RPV PO	↔ diazepam expected	No dose adjustment needed.
	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	DOR, ETR, NVP, RPV IM, RPV PO	↔ lorazepam expected	No dose adjustment needed.
	EFV	↔ lorazepam AUC	No dose adjustment needed.
Midazolam	DOR	↔ midazolam AUC	No dose adjustment needed.
	EFV	↑ or ↓ midazolam possible	Monitor for therapeutic effectiveness and toxicity of midazolam.
	ETR	Midazolam AUC ↓ 31% Midazolam active metabolite C_{max} ↑ 57%	Monitor for therapeutic effectiveness of midazolam.
	NVP	↓ midazolam possible	Monitor for therapeutic effectiveness of midazolam.
	RPV IM, RPV PO	↔ midazolam expected	No dose adjustment needed.

[a] R-methadone is the active form of methadone.

Key to Symbols

↑ = increase
↓ = decrease
↔ = no change

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Key: ARV = antiretroviral; AUC = area under the curve; C_{max} = maximum plasma concentration; C_{min} = minimum plasma concentration; CAB = cabotegravir; CCB = calcium channel blocker; DAA = direct-acting antiviral; DHA = dihydroartemisinin; DOR = doravirine; EFV = efavirenz; ETR = etravirine; HCV = hepatitis C virus; IM = intramuscular; INR = international normalized ratio; isoniazid = isonicotinic acid hydrazide; MAC = *Mycobacterium avium* complex; MPA = medroxyprogesterone acetate; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; OH-itraconazole = active metabolite of itraconazole; PCP = *Pneumocystis jirovecii* pneumonia; PDE5 = phosphodiesterase type 5; PI/r = protease inhibitor/ritonavir; PO = orally; QTc = QT corrected for heart rate; RPV = rilpivirine; RTV = ritonavir.

Table 24c. Drug Interactions between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents)

This table provides information on the known or predicted interactions between nucleoside reverse transcriptase inhibitors (NRTIs) and non-antiretroviral drugs.

Recommendations for managing a particular drug interaction may differ depending on whether a new antiretroviral (ARV) drug is being initiated in a patient on a stable concomitant medication or whether a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgement to select the most appropriate alternative medication to use.

Interactions associated with zidovudine are **not** included in this table. Please refer to the U.S. Food and Drug Administration product labels for information regarding drug interactions between these NRTIs and other drugs.

Concomitant Drug	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antimycobacterials			
Rifabutin	TAF	↓ TAF possible	Do not coadminister unless benefits outweigh risks. If coadministered, monitor for virologic response.
	TDF	↔ AUC TFV	No dose adjustment needed.
Rifampin	TAF	TAF with Rifampin Compared with TDF Alone • TFV-DP AUC ↑ 4.2-fold TAF with Rifampin Compared with TAF Alone • TAF AUC ↓ 55% • TFV-DP AUC ↓ 36% TAF 25 mg Twice Daily with Rifampin Compared with TAF Once Daily Alone • TAF AUC ↓ 14% • TFV-DP AUC ↓ 24%	Do not coadminister unless benefits outweigh risks. Intracellular TFV-DP levels are higher when TAF is coadministered with rifampin than when TDF is administered alone, but clinical outcomes have not been studied. If coadministered, monitor virologic response.
	TDF	↔ AUC TFV	No dose adjustment needed.
Rifapentine	TAF	↓ TAF possible	Do not coadminister unless benefits outweigh risks. If coadministered, monitor for virologic response.
	TDF	↔ AUC TFV	No dose adjustment needed.
Antivirals—Orthopoxviruses (Smallpox, Mpox)			
Brincidofovir	All NRTIs	↔ brincidofovir expected	No dose adjustment needed.

Table 24c. Drug Interactions between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Cidofovir	ABC, 3TC, FTC, TAF	↔ cidofovir expected	No dose adjustment needed.
	TDF	↑ TDF and cidofovir possible	Potential for renal toxicity when TDF is given with a nephrotoxic agent, such as cidofovir. If concomitant use is necessary, closely monitor renal function.
Tecovirimat	All NRTIs	↔ tecovirimat expected	No dose adjustment needed.
Cytomegalovirus and Hepatitis B Antivirals			
Adefovir	TAF, 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.
Hormonal Therapies			
17-β-estradiol	FTC	FTC AUC ↓ 14% to 24%	No dose adjustment needed.
	TDF	TFV AUC ↓ 12% to 27%	No dose adjustment needed.
Other hormones used for contraception, gender affirming therapy, or menopausal replacement therapy	All NRTIs	No change expected.	No dose adjustment needed.
Hepatitis C Antiviral Agents			
Glecaprevir/Pibrentasvir	TAF	↔ TFV AUC	No dose adjustment needed.
	TDF	TFV AUC ↑ 29%	No dose adjustment needed.
Ledipasvir/Sofosbuvir	TAF	TFV AUC ↑ 27%	No dose adjustment needed.

Table 24c. Drug Interactions between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	TDF	Ledipasvir ↑ TFV AUC 35% to 98% when TDF is given with various PIs and NNRTIs. Ledipasvir ↑ TFV C_{min} 55% to 80% when TDF is given with various PIs, NNRTIs, or INSTIs. Further ↑ TFV AUC and C_{max} possible when TDF, ledipasvir/sofosbuvir, and PIs are coadministered.	Do not coadminister with EVG/c, TDF, or FTC. If TDF is used, monitor for TDF toxicities. Consider using TAF in patients at risk of TDF-associated adverse events. Consider using TAF or alternative HCV therapy in patients on TDF plus a PI/r or PI/c. The safety of increased TFV exposure with this combination has not been established.
Ribavirin	TDF	Ribavirin with Sofosbuvir 400 mg • ↔ TFV AUC	No dose adjustment needed.
Sofosbuvir/Velpatasvir	TAF	↔ TFV expected	No dose adjustment needed.
	TDF	TFV C_{max} ↑ 44% to 46% and AUC ↑ 40% when coadministered with various ARV combinations.	If TDF is used in these patients, monitor for TDF-related toxicities. Consider using TAF in patients at risk of TDF-related adverse events.
Sofosbuvir/Velpatasvir/ Voxilaprevir	TAF	↔ TAF expected	No dose adjustment needed.
	TDF	TFV C_{max} ↑ 48% and AUC ↑ 39% when coadministered with various ARV combinations.	If TDF is used in these patients, monitor for TDF-related toxicities. Consider using TAF in patients at risk of TDF-related adverse events.
Narcotics and Treatment for Opioid Dependence			
Buprenorphine	3TC, TDF	↔ 3TC, TDF, and buprenorphine	No dose adjustment needed.
	TAF	↔ TAF expected	No dose adjustment needed.
Methadone	ABC	Methadone clearance ↑ 22%	No dose adjustment needed.

Table 24c. Drug Interactions between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Other Drugs			
Anticonvulsants Carbamazepine, oxcarbazepine, phenobarbital, phenytoin	TAF	With Carbamazepine • TAF AUC ↓ 55% • ↓ TAF possible with other anticonvulsants	Do not coadminister.
Riociguat	ABC	Riociguat AUC ↑ 200%	If coadministered, initiate riociguat at 0.5 mg three times daily and monitor for riociguat-related adverse effects (e.g., hypotension).
St. John's Wort	TAF	↓ TAF possible	Do not coadminister.
Antiretroviral Drugs			
Capsid Inhibitor			
LEN (SQ and PO)	ABC, FTC, 3TC	↔ ABC, FTC, 3TC, LEN expected	No dose adjustment needed.
	TAF	TAF AUC ↑ 32% ↔ LEN	No dose adjustment needed.
	TDF	TDF AUC ↑ 47% ↔ LEN	No dose adjustment needed.
INSTIs			
DTG	TAF	↔ TAF AUC	No dose adjustment needed.
	TDF	↔ TDF AUC ↔ DTG AUC	No dose adjustment needed.
RAL	TDF	RAL AUC ↑ 49%	No dose adjustment needed.
PIs			
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 needed (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%	Do not coadminister unboosted ATV with TDF. Use ATV 300 mg plus (RTV 100 mg or COBI 150 mg) daily when coadministering TDF 300 mg daily. If using TDF and an H2 receptor antagonist in an ART-experienced

Table 24c. Drug Interactions between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
			patient, use ATV 400 mg plus (RTV 100 mg or COBI 150 mg) daily Monitor for TDF-associated toxicities.
DRV/c	TAF	TAF 25 mg with DRV/c • ↔ TAF	No dose adjustment needed.
	TDF	TFV ↑ possible	Monitor for TDF-associated toxicities.
DRV/r	TAF	TAF 10 mg with DRV/r • ↔ TAF AUC	No dose adjustment needed.
	TDF	TFV AUC ↑ 22% and C_{min} ↑ 37%	Clinical significance is unknown. If coadministered, monitor for TDF-associated toxicities.
LPV/r	TAF	TAF 10 mg with LPV/r • TAF AUC ↑ 47%	No dose adjustment needed.
	TDF	↔ LPV/r AUC TFV AUC ↑ 32%	Clinical significance is unknown. If coadministered, monitor for TDF-associated toxicities.

Key to Symbols

↑ = increase
↓ = decrease
↔ = no change

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; C_{min} = minimum plasma concentration; COBI = cobicistat; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; HCV = hepatitis C virus; INSTI = integrase strand transfer inhibitor; LEN = lenacapavir; LPV/r = lopinavir/ritonavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; RAL = raltegravir; RTV = ritonavir; SQ = subcutaneous; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TFV = tenofovir; TFV-DP = tenofovir diphosphate

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

This table provides information on the known or predicted interactions between integrase strand transfer inhibitors (INSTIs) (bictegravir [BIC], dolutegravir [DTG], elvitegravir [EVG], or raltegravir [RAL]) and non-antiretroviral (ARV) drugs. EVG is always coadministered with cobicistat. Cabotegravir (CAB) intramuscular (IM) plus rilpivirine (RPV) IM are co-packaged into a single product and are coadministered as a complete regimen; therefore, the dosing recommendations and clinical comments reflect the combination of CAB IM and RPV IM treatments. Drug interaction studies were not conducted with either CAB IM or RPV IM. Drug interaction studies with oral CAB and RPV were leveraged to make the dosing recommendations for CAB IM and RPV IM. For information regarding interactions between INSTIs and other ARV drugs, including dosing recommendations, refer to Tables 24c, 24e, 24f, and 25b.

Recommendations for managing a particular drug interaction may differ, depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or whether a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgement to select the most appropriate alternative medication to use.

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers			
Al, Mg, +/– Ca-Containing Antacids Please refer to the Miscellaneous Drugs section of this table for recommendations on use with other polyvalent cation products (e.g., Fe and Ca supplements, multivitamins).	BIC	Al/Mg Hydroxide Antacid • ↔ BIC AUC if antacid is administered 2 hours after BIC and under fasting conditions • BIC AUC ↓ 52% if antacid is administered 2 hours before BIC • BIC AUC ↓ 47% to 79% if administered simultaneously with antacid $CaCO_3$ Antacid • ↔ BIC AUC if administered with food • BIC AUC ↓ 33% if administered under fasting conditions	With Antacids That Contain Al/Mg • Administer antacids that contain Al/Mg at least 2 hours after or 6 hours before BIC. With Antacids That Contain Ca • Administer BIC and antacids that contain Ca together with food. • Do not coadminister BIC simultaneously with antacids that contain Ca on an empty stomach.
	CAB PO	CAB PO ↓ expected	With Antacids That Contain Polyvalent Cations (Al, Mg, or Ca) • Administer antacid products at least 2 hours before or 4 hours after taking CAB PO.
	CAB IM	↔ CAB IM expected	No dose adjustment needed.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	DTG	DTG AUC ↓ 74% if administered simultaneously with antacid DTG AUC ↓ 26% if administered 2 hours before antacid	Administer DTG at least 2 hours before or at least 6 hours after antacids that contain polyvalent cations.
	EVG/c	EVG AUC ↓ 40% to 50% if administered simultaneously with antacid EVG AUC ↓ 15% to 20% if administered 2 hours before or after antacid; ↔ with a 4-hour interval	Separate EVG/c and antacid administration by more than 2 hours.
	RAL	Al/Mg Hydroxide Antacid • RAL C_{min} ↓ 49% to 63% $CaCO_3$ Antacid • RAL 400 mg twice daily: C_{min} ↓ 32% • RAL 1,200 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 1,200 mg once daily: Do not coadminister. • RAL 400 mg twice daily: No dose adjustment or separation needed.
H2-Receptor Antagonists	BIC, CAB (PO and IM), DTG, EVG/c	↔ INSTI	No dose adjustment needed.
	RAL	RAL AUC ↑ 44% and C_{max} ↑ 60%	No dose adjustment needed.
Proton Pump Inhibitors	BIC, CAB (PO and IM), DTG, EVG/c	↔ INSTI	No dose adjustment needed.
	RAL	RAL AUC ↑ 37% and C_{min} ↑ 24%	No dose adjustment needed.
Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia			
Alfuzosin	BIC, CAB (PO and IM), DTG, RAL	↔ alfuzosin expected	No dose adjustment needed.
	EVG/c	↑ alfuzosin expected	Contraindicated.
Doxazosin	BIC, CAB (PO and IM), DTG, RAL	↔ doxazosin expected	No dose adjustment needed.
	EVG/c	↑ doxazosin possible	Initiate doxazosin at lowest dose. Titrate based on doxazosin efficacy and adverse events. Doxazosin dose reduction may be needed.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Tamsulosin	BIC, CAB (PO and IM), DTG, RAL	↔ tamsulosin expected	No dose adjustment needed.
	EVG/c	↑ tamsulosin expected	Do not coadminister unless the benefits outweigh the risks. If coadministered, monitor for tamsulosin-related adverse events.
Terazosin	BIC, CAB (PO and IM), DTG, RAL	↔ terazosin expected	No dose adjustment needed.
	EVG/c	↑ terazosin possible	Initiate terazosin at lowest dose. Titrate based on terazosin efficacy and adverse events. Terazosin dose reduction may be necessary.
Silodosin	BIC, CAB (PO and IM), DTG, RAL	↔ silodosin expected	No dose adjustment needed.
	EVG/c	↑ silodosin expected	Contraindicated.
Antibacterials - Antimycobacterials			
Rifabutin	BIC	Rifabutin 300 mg Once Daily • BIC AUC ↓ 38% and C_{min} ↓ 56%	Do not coadminister.
	CAB PO	CAB PO AUC ↓ 23% and C_{min} ↓ 26% ↔ rifabutin	No dose adjustment needed.
	CAB IM	↓ CAB IM and RPV expected ↔ rifabutin expected	Contraindicated due to ↓ RPV, which is co-packaged and coadministered with CAB IM.
	DTG	Rifabutin 300 mg Once Daily • ↔ DTG AUC and C_{min} ↓ 30%	No dose adjustment needed.
	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 needed.
Rifampin	BIC	BIC AUC ↓ 75%	Contraindicated.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	CAB PO	CAB PO AUC ↓ 59% and C_{min} ↓ 50%	Contraindicated.
	CAB IM	CAB IM ↓ expected	Contraindicated.
	DTG	Rifampin With DTG 50 mg Twice Daily Compared to DTG 50 mg Twice Daily Alone • DTG AUC ↓ 54% and C_{min} ↓ 72% Rifampin With DTG 50 mg Twice Daily Compared to DTG 50 mg Once Daily Alone • DTG AUC ↑ 33% and C_{min} ↑ 22%	Use DTG 50 mg twice daily (instead of DTG 50 mg once daily) in patients without suspected or documented INSTI-associated resistance mutations. Consider an alternative to rifampin, such as rifabutin, in patients with certain suspected or documented INSTI-associated resistance mutations.
	EVG/c	Significant ↓ EVG and COBI expected	Contraindicated.
	RAL	RAL 400 mg • RAL AUC ↓ 40% and C_{min} ↓ 61% Rifampin With RAL 800 mg Twice Daily Compared to RAL 400 mg Twice Daily Alone • RAL AUC ↑ 27% and C_{min} ↓ 53%	Use RAL 800 mg twice daily instead of 400 mg twice daily. Do not coadminister RAL 1,200 mg once daily with rifampin. Monitor closely for virologic response or consider using rifabutin as an alternative rifamycin.
Rifapentine	BIC, EVG/c	Significant ↓ BIC, EVG, and COBI expected	Do not coadminister.
	CAB (PO and IM)	Significant ↓ CAB (PO and IM) expected	Contraindicated.
	DTG	Rifapentine 900 mg Once Weekly • DTG AUC ↓ 26% and C_{min} ↓ 47%	With once-weekly rifapentine, DTG 50 mg daily may be used in patients with viral suppression on daily DTG. Monitor for virologic efficacy. Do not coadminister in patients who require twice-daily DTG. Do not coadminister DTG with once-daily rifapentine.
	RAL	Rifapentine 900 mg Once Weekly • RAL AUC ↑ 71% and C_{min} ↓ 12% Rifapentine 600 mg Once Daily • RAL C_{min} ↓ 41%	For once-weekly rifapentine and RAL 400 mg twice daily, no dose adjustment is needed. Do not coadminister with once-daily rifapentine.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antibacterials - Macrolides			
Azithromycin	All INSTIs	↔ azithromycin expected	No dose adjustment needed.
Clarithromycin	BIC	↑ BIC possible	No dose adjustment needed.
	CAB (PO and IM), DTG, RAL	↔ clarithromycin expected	No dose adjustment needed.
	EVG/c	↑ clarithromycin expected ↑ COBI possible	Reduce clarithromycin dose by 50% in patients with CrCl 50 to 60 mL/min. Do not coadminister in patients with CrCl <50 mL/min. Consider alternative ARV or use azithromycin.
Erythromycin	BIC	↑ BIC possible	No dose adjustment needed.
	CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ erythromycin expected	No dose adjustment needed.
	EVG/c	↑ erythromycin expected ↑ COBI possible	No data available for dose recommendation. Consider alternative ARV or use azithromycin.
Anticoagulants			
Apixaban	BIC, CAB (PO and IM), DTG, RAL	↔ apixaban expected	No dose adjustment needed.
	EVG/c	↑ apixaban expected	Do not coadminister in patients who require apixaban 2.5 mg twice daily. Reduce apixaban dose by 50% in patients who require apixaban 5 mg or 10 mg twice daily.
Dabigatran	BIC, CAB (PO and IM), DTG, RAL	↔ dabigatran expected	No dose adjustment needed.
	EVG/c	↑ dabigatran expected With COBI 150 mg Alone • Dabigatran AUC ↑ 110% to 127%	Dabigatran dosing recommendation depends on indication and renal function. Refer to dabigatran prescribing information for dosing instructions when using dabigatran concomitantly with P-glycoprotein inhibitors.
Edoxaban	BIC, CAB (PO and IM), DTG, RAL	↔ edoxaban expected	No dose adjustment needed.
	EVG/c	↑ edoxaban expected	Stroke Prevention in Nonvalvular Atrial Fibrillation • No dose adjustment needed. Deep Venous Thrombosis and Pulmonary Embolism • Administer edoxaban 30 mg once daily.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Rivaroxaban	BIC, CAB (PO and IM), DTG, RAL	↔ rivaroxaban expected	No dose adjustment needed.
	EVG/c	↑ rivaroxaban expected	Do not coadminister.
Warfarin	BIC, CAB (PO and IM), DTG, RAL	↔ warfarin expected	No dose adjustment needed.
	EVG/c	↑ or ↓ warfarin possible	Monitor INR and adjust warfarin dose accordingly.
Anticonvulsants			
Carbamazepine	BIC	↓ BIC possible	Do not coadminister.
	CAB (PO and IM)	↓ CAB expected	Contraindicated.
	DTG	DTG AUC ↓ 49%	Increase DTG dose to 50 mg twice daily in ART-naive or ART-experienced (but INSTI-naive) patients. Do not coadminister in INSTI-experienced patients with known or suspected INSTI resistance.
	EVG/c	Carbamazepine AUC ↑ 43% EVG AUC ↓ 69% and C_{min} ↓ >99% ↓ COBI expected	Contraindicated.
	RAL	↓ or ↔ RAL possible	Do not coadminister.
Eslicarbazepine	All INSTIs	↓ INSTI possible ↓ COBI possible	Consider alternative ARV or anticonvulsant.
Ethosuximide	BIC, CAB (PO and IM), DTG, RAL	↔ ethosuximide expected	No dose adjustment needed.
	EVG/c	↑ ethosuximide possible	Monitor for ethosuximide-related adverse events.
Lamotrigine	BIC, CAB (PO and IM), DTG, RAL	↔ lamotrigine expected	No dose adjustment needed.
	EVG/c	No data	Monitor anticonvulsant concentrations and adjust dose accordingly.
Oxcarbazepine	BIC, DTG	↓ BIC and DTG possible	Do not coadminister.
	CAB (PO and IM)	↓ CAB expected	Contraindicated.
	EVG/c, RAL	↓ EVG/c and RAL possible	Consider alternative ARV or anticonvulsant.
Phenobarbital, Phenytoin	BIC, DTG, RAL	↓ BIC and DTG possible ↓ or ↔ RAL possible	Do not coadminister.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	CAB (PO and IM), EVG/c	↓ CAB and EVG/c expected	Contraindicated.
Valproic Acid	All INSTIs	No data	Monitor valproic acid concentration and virologic response.
Antidepressants, Anxiolytics, and Antipsychotics Also see the Sedative/Hypnotics section below			
Bupropion	BIC, CAB (PO and IM), DTG, RAL	↔ bupropion expected	No dose adjustment needed.
	EVG/c	↑ bupropion possible	Titrate bupropion dose based on clinical response.
Buspirone	BIC, CAB (PO and IM), DTG, RAL	↔ buspirone expected	No dose adjustment needed.
	EVG/c	↑ buspirone possible	Initiate buspirone at a low dose. Buspirone dose reduction may be needed.
Nefazodone	BIC, CAB (PO and IM), DTG, RAL	↔ nefazodone expected	No dose adjustment needed.
	EVG/c	↑ nefazodone expected	Consider alternative ARV or antidepressant.
Trazodone	BIC, CAB (PO and IM), DTG, RAL	↔ trazodone expected	No dose adjustment needed.
Tricyclic Antidepressants Amitriptyline, desipramine, doxepin, imipramine, nortriptyline	BIC, CAB (PO and IM), DTG, RAL	↔ TCA expected	No dose adjustment needed.
	EVG/c	Desipramine AUC ↑ 65%	Initiate with lowest dose of TCA and titrate dose carefully.
		↑ TCA expected	Initiate with lowest dose of TCA. Titrate dose carefully based on antidepressant response and/or drug concentrations.
Selective Serotonin Reuptake Inhibitors Citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline	EVG/c	↔ sertraline	No dose adjustment needed.
	EVG/c	↑ other SSRIs possible	Initiate with lowest dose of SSRI. Titrate dose carefully based on antidepressant response.
	BIC, CAB (PO and IM), DTG, RAL	↔ SSRI expected	No dose adjustment needed.
Antipsychotics			
Aripiprazole	BIC, CAB (PO and IM), DTG, RAL	↔ aripiprazole expected	No dose adjustment needed.
	EVG/c	↑ aripiprazole expected	Administer 25% of the usual aripiprazole dose. Titrate based on aripiprazole efficacy and adverse events. Refer to aripiprazole label for dosing recommendations

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
			in patients who are known to be CYP2D6 poor metabolizers or who have major depressive disorder.
Brexpiprazole	BIC, CAB (PO and IM), DTG, RAL	↔ brexpiprazole expected	No dose adjustment needed.
	EVG/c	↑ brexpiprazole expected	Administer 25% of the usual brexpiprazole dose. Titrate based on brexpiprazole efficacy and adverse events. Refer to brexpiprazole label for dosing recommendations in patients who are known to be CYP2D6 poor metabolizers or who have major depressive disorder.
Cariprazine	BIC, CAB (PO and IM), DTG, RAL	↔ cariprazine expected	No dose adjustment needed.
	EVG/c	↑ cariprazine expected	Starting Cariprazine in a Patient Who Is Already Receiving 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 cariprazine 1.5 mg daily. Dose can be increased to a maximum of cariprazine 3 mg daily. If EVG/c is withdrawn, cariprazine dose may need to be increased. Starting EVG/c in a Patient Who Is Already Receiving Cariprazine • For patients receiving cariprazine 3 mg or cariprazine 6 mg daily, reduce the dose by half. For patients receiving cariprazine 4.5 mg daily, reduce dose to cariprazine 1.5 mg or cariprazine 3 mg daily. For patients receiving cariprazine 1.5 mg daily, change to cariprazine 1.5 mg every other day. If EVG/c is withdrawn, cariprazine dose may need to be increased.
Iloperidone	BIC, CAB (PO and IM), DTG, RAL	↔ iloperidone expected	No dose adjustment needed.
	EVG/c	↑ iloperidone expected	Decrease iloperidone dose by 50%.
Lumateperone	BIC, CAB (PO and IM), DTG, RAL	↔ lumateperone expected	No dose adjustment needed.
	EVG/c	↑ lumateperone expected	Do not coadminister.
Lurasidone	BIC, CAB (PO and IM), DTG, RAL	↔ lurasidone expected	No dose adjustment needed.
	EVG/c	↑ lurasidone expected	Contraindicated.
Olanzapine	All INSTIs	↔ olanzapine expected	No dose adjustment needed.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Other Antipsychotics CYP3A4 and/or CYP2D6 substrates (e.g., perphenazine, risperidone, thioridazine)	EVG/c	↑ antipsychotic possible	Initiate antipsychotic at a low dose. Antipsychotic dose reduction may be needed.
Pimavanserin	BIC, CAB (PO and IM), DTG, RAL	↔ pimavanserin expected	No dose adjustment needed.
	EVG/c	↑ pimavanserin expected	Reduce pimavanserin dose to 10 mg.
Pimozide	BIC, CAB (PO and IM), DTG, RAL	↔ pimozide expected	No dose adjustment needed.
	EVG/c	↑ pimozide expected	Contraindicated.
Quetiapine	BIC, CAB (PO and IM), DTG, RAL	↔ quetiapine expected	No dose adjustment needed.
	EVG/c	↑ quetiapine AUC expected	Starting Quetiapine in a Patient Receiving EVG/c • Start quetiapine at the lowest dose and titrate up as needed. Monitor for quetiapine efficacy and adverse events. Starting EVG/c in a Patient Receiving a Stable Dose of Quetiapine • Reduce quetiapine dose to 1/6 of the current dose. Closely monitor for quetiapine efficacy and adverse events.
Ziprasidone	BIC, CAB (PO and IM), DTG, RAL	↔ ziprasidone expected	No dose adjustment needed.
	EVG/c	↑ ziprasidone possible	Monitor for ziprasidone-related adverse events.
Antifungals			
Isavuconazole	BIC, CAB (PO and IM), DTG, RAL	↑ INSTI possible	No dose adjustment needed.
	EVG/c	↑ isavuconazole expected ↑ or ↓ EVG and COBI possible	If coadministered, consider monitoring isavuconazole concentrations and assessing virologic response.
Itraconazole	BIC	↑ BIC expected	No dose adjustment needed.
	CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ itraconazole expected	No dose adjustment needed.
	EVG/c	↑ itraconazole expected ↑ EVG and COBI possible	Consider monitoring itraconazole concentrations to guide dose adjustments. Do not coadminister with

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
			high itraconazole doses (>200 mg/day) unless guided by itraconazole concentrations.
Posaconazole	BIC	↑ BIC expected	No dose adjustment needed.
	CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ posaconazole expected	No dose adjustment needed.
	EVG/c	↑ EVG and COBI possible ↑ posaconazole possible	If coadministered, monitor posaconazole concentrations.
Voriconazole	BIC	↑ BIC possible	No dose adjustment needed.
	CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ voriconazole expected	No dose adjustment needed.
	EVG/c	↑ voriconazole expected ↑ EVG and COBI possible	Do not coadminister voriconazole and COBI, unless the benefit outweighs the risk. If coadministered, consider monitoring voriconazole concentrations and adjust dose accordingly.
Antihyperglycemics			
Metformin	BIC	Metformin AUC ↑ 39%	Monitor for adverse events of metformin.
	DTG	DTG 50 mg Once Daily plus Metformin 500 mg Twice Daily • Metformin AUC ↑ 79% and C_{max} ↑ 66% DTG 50 mg Twice Daily plus Metformin 500 mg Twice Daily • Metformin AUC ↑ 2.4-fold and C_{max} ↑ 2-fold	Start metformin at the lowest dose and titrate based on glycemic control. Monitor for adverse events of metformin. When starting/stopping DTG in patients on metformin, dose adjustment of metformin may be necessary to maintain optimal glycemic control and/or minimize adverse events of metformin.
	CAB (PO and IM), RAL	↔ metformin expected	No dose adjustment needed.
Saxagliptin	BIC, CAB (PO and IM), DTG, RAL	↔ saxagliptin expected	No dose adjustment needed.
	EVG/c	↑ saxagliptin expected	Limit saxagliptin dose to 2.5 mg once daily.
Dapagliflozin/ Saxagliptin	BIC, CAB (PO and IM), DTG, RAL	↔ dapagliflozin or saxagliptin expected	No dose adjustment needed.
	EVG/c	↑ saxagliptin expected	Do not coadminister. Dapagliflozin is available only as a coformulated drug that contains 5 mg of saxagliptin. When coadministered with EVG/c, the dose of saxagliptin should not exceed 2.5 mg once daily; thus, this combination is not recommended.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antiplatelets			
Clopidogrel	BIC, CAB (PO and IM), DTG, RAL	↔ clopidogrel expected	No dose adjustment needed.
	EVG/c	↓ clopidogrel active metabolite, with impaired platelet inhibition expected	Do not coadminister.
Prasugrel	BIC, CAB (PO and IM), DTG, RAL	↔ prasugrel expected	No dose adjustment needed.
	EVG/c	↓ prasugrel active metabolite, with no impairment of platelet inhibition expected	No dose adjustment needed.
Ticagrelor	BIC, CAB (PO and IM), DTG, RAL	↔ ticagrelor expected	No dose adjustment needed.
	EVG/c	↑ ticagrelor expected	Do not coadminister.
Vorapaxar	BIC, CAB (PO and IM) DTG, RAL	↔ vorapaxar expected	No dose adjustment needed.
	EVG/c	↑ vorapaxar expected	Do not coadminister.
Antivirals—Orthopoxviruses (Smallpox, Mpox)			
Brincidofovir	BIC, CAB (PO and IM), DTG, RAL	↔ INSTI expected	No dose adjustment needed.
	EVG/c	↑ brincidofovir possible ↑ EVG possible	Administer EVG/c dose at least 3 hours after administering brincidofovir and monitor for brincidofovir-related adverse events (i.e., elevations in ALT/AST and bilirubin and GI adverse events).
Cidofovir	BIC, CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ cidofovir expected	No dose adjustment needed.
Tecovirimat	CAB (IM)	↔ CAB expected	No dose adjustment needed. Do not initiate CAB/RPV IM during or within 2 weeks after tecovirimat treatment. (Refer to Table 24b for interaction with RPV.)
	BIC, CAB (PO), DTG, EVG/c, RAL	↔ INSTI expected	No dose adjustment needed.
Beta-Agonists, Long-Acting Inhaled			
Arformoterol, Formoterol	All INSTIs	↔ arformoterol or formoterol expected	No dose adjustment needed.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Indacaterol	BIC, CAB (PO and IM), DTG, RAL	↔ indacaterol expected	No dose adjustment needed.
	EVG/c	↑ indacaterol expected	
Olodaterol	BIC, CAB (PO and IM), DTG, RAL	↔ olodaterol expected	No dose adjustment needed.
	EVG/c	↑ olodaterol expected	
Salmeterol	BIC, CAB (PO and IM), DTG, RAL	↔ salmeterol expected	No dose adjustment needed.
	EVG/c	↑ salmeterol possible	Do not coadminister due to the potential for increased risk of salmeterol-associated cardiovascular events.
Cardiac Medications			
Amiodarone	BIC, CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ amiodarone expected	No dose adjustment needed.
	EVG/c	↑ INSTI possible ↑ amiodarone possible	Do not coadminister unless the benefits outweigh the risks. If coadministration is necessary, monitor for amiodarone-related adverse events and consider monitoring ECG and amiodarone concentrations.
Bepridil, Digoxin, Disopyramide, Dronedarone, Flecainide, Systemic Lidocaine, Mexilitine, Propafenone, Quinidine	BIC, CAB (PO and IM), DTG	↔ expected for the listed antiarrhythmics, except for disopyramide ↑ disopyramide possible	No dose adjustment needed. Monitor for disopyramide-related adverse events.
	RAL	↔ expected for the listed antiarrhythmics	No dose adjustment needed.
	EVG/c	↑ antiarrhythmics possible Digoxin C_{max} ↑ 41% and ↔ AUC	Therapeutic drug monitoring for antiarrhythmics, if available, is recommended.
Beta Blockers (e.g., metoprolol, timolol)	BIC, CAB (PO and IM), DTG, RAL	↔ beta blocker expected	No dose adjustment needed.
	EVG/c	↑ beta blocker possible	Beta blocker dose may need to be decreased; adjust dose based on clinical response. Consider using an alternative ARV or a beta blocker that is not metabolized by CYP450 enzymes (e.g., atenolol, labetalol, nadolol, sotalol).
Bosentan	BIC, DTG	↓ BIC and DTG possible	No dose adjustment needed.
	CAB (PO and IM)	↔ bosentan expected	Consider using alternative ARV or an alternative to bosentan because bosentan may ↓ RPV, which is co-packaged and coadministered with CAB IM. If

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
			bosentan is used with RPV, monitor virologic response to ART.
	RAL	↔ bosentan expected	No dose adjustment needed.
	EVG/c	↑ bosentan possible	In Patients on EVG/c **≥10 Days** • Start bosentan at 62.5 mg once daily or every other day based on individual tolerability. In Patients on Bosentan Who Require EVG/c • Stop bosentan ≥36 hours before EVG/c initiation. At least 10 days after initiation of EVG/c, resume bosentan at 62.5 mg once daily or every other day based on individual tolerability.
Calcium Channel Blockers	BIC	↑ BIC possible with diltiazem ↔ expected for all other CCBs	No dose adjustment needed.
	CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ CCB expected	No dose adjustment needed.
	EVG/c	↑ CCB possible	Titrate CCB dose and monitor for CCB efficacy and adverse events.
Dofetilide	BIC, DTG	↑ dofetilide expected	Contraindicated.
	CAB (PO and IM), RAL	↔ dofetilide expected	No dose adjustment needed.
	EVG/c	↑ dofetilide possible	Do not coadminister.
Eplerenone	BIC, CAB (PO and IM), DTG, RAL	↔ eplerenone expected	No dose adjustment needed.
	EVG/c	↑ eplerenone expected	Contraindicated.
Ivabradine	BIC, CAB (PO and IM), DTG, RAL	↔ ivabradine expected	No dose adjustment needed.
	EVG/c	↑ ivabradine expected	Contraindicated.
Ranolazine	BIC, CAB (PO and IM), DTG, RAL	↔ ranolazine expected	No dose adjustment needed.
	EVG/c	↑ ranolazine expected	Contraindicated.
Corticosteroids			
Beclomethasone Inhaled or intranasal	BIC, CAB (PO and IM), DTG, EVG/c, RAL	↔ glucocorticoid expected	No dose adjustment needed.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

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

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Dasabuvir plus Ombitasvir/Paritaprevir/RTV	BIC	↔ BIC expected	No dose adjustment needed.
	CAB (PO and IM)	↔ CAB expected ↑ RPV IM expected	Do not coadminister due to potential for QTc prolongation with higher concentrations of RPV. RPV is co-packaged and coadministered with CAB IM.
	DTG	↔ DTG, dasabuvir, plus ombitasvir/paritaprevir/RTV	No dose adjustment needed.
	EVG/c	No data	Do not coadminister.
	RAL	RAL AUC ↑ 134%	No dose adjustment needed.
Elbasvir/Grazoprevir	BIC	↔ BIC expected	No dose adjustment needed.
	CAB (PO and IM)	↔ CAB, elbasvir, and grazoprevir expected	No dose adjustment needed.
	DTG	↔ DTG ↔ elbasvir ↔ grazoprevir	No dose adjustment needed.
	EVG/c	↑ elbasvir expected ↑ grazoprevir expected	Do not coadminister.
	RAL	↔ RAL with elbasvir RAL AUC ↑ 43% with grazoprevir ↔ elbasvir ↔ grazoprevir	No dose adjustment needed.
Glecaprevir/Pibrentasvir	BIC, CAB (PO and IM)	↔ BIC or CAB expected	No dose adjustment needed.
	DTG	↔ DTG and glecaprevir/pibrentasvir	No dose adjustment needed.
	RAL	No significant effect RAL AUC ↑ 47%	
	EVG/c	Glecaprevir AUC ↑ 3-fold Pibrentasvir AUC ↑ 57% EVG AUC ↑ 47%	No dose adjustment needed. If coadministered with TDF, monitor for TDF-related adverse events. Consider monitoring for hepatotoxicity if coadministered with TDF or TAF.
Ledipasvir/Sofosbuvir	BIC, DTG, RAL	↔ BIC, DTG, and RAL	No dose adjustment needed.
	CAB (PO and IM)	↔ CAB expected	No dose adjustment needed.
	EVG/c/TDF/FTC	↑ TDF expected ↑ ledipasvir expected	Do not coadminister.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	EVG/c/TAF/FTC	↔ EVG/c/TAF/FTC expected	No dose adjustment needed.
Sofosbuvir	BIC, CAB (PO and IM), DTG, EVG/C	↔ INSTI expected ↔ sofosbuvir expected	No dose adjustment needed.
	RAL	↔ RAL and sofosbuvir	No dose adjustment needed.
Sofosbuvir/Velpatasvir	BIC, DTG, RAL	↔ sofosbuvir and velpatasvir	No dose adjustment needed. If coadministered with TDF, monitor for TDF-related adverse events.
	CAB (PO and IM)	↔ CAB expected ↔ sofosbuvir and velpatasvir expected	
	EVG/c	↔ EVG/c/TAF/FTC Velpatasvir AUC ↑ 50%	
Sofosbuvir/ Velpatasvir/ Voxilaprevir	BIC	When Administered With Sofosbuvir/ Velpatasvir/ Voxilaprevir (400 mg/100 mg/100 mg) plus Voxilaprevir 100 mg • ↔ BIC, sofosbuvir, velpatasvir, voxilaprevir	No dose adjustment needed.
	EVG/c	When Administered 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 needed. If coadministered with TDF, monitor for TDF-related adverse events. Consider monitoring for hepatotoxicity if coadministered with TDF or TAF.
	BIC, CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ sofosbuvir, velpatasvir, and voxilaprevir expected	No dose adjustment needed.
Herbal Products			
St. John's Wort	BIC, CAB (PO and IM), DTG	↓ BIC and DTG possible	Do not coadminister.
	EVG/c	↓ EVG and COBI expected	Contraindicated.
Hormonal Therapies			
Contraceptives: Non-Oral	BIC, CAB (PO and IM), DTG, RAL	Etonogestrel (subdermal implant) ↑ 27% with DTG	No dose adjustment needed.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
		↔ expected with BIC, CAB, RAL	
	EVG/c	No data	No data available to make dose recommendation.
Contraceptives: Oral	BIC, DTG, RAL	↔ ethinyl estradiol and norgestimate ↔ INSTI	No dose adjustment needed.
	CAB (PO and IM)	↔ ethinyl estradiol and levonorgestrel with CAB PO	No dose adjustment needed.
	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 may include insulin resistance, dyslipidemia, acne, and venous thrombosis. Decreased ethinyl estradiol may lead to more intermenstrual bleeding. Weigh the risks and benefits of using the drug and consider using an alternative ARV or contraceptive method.
		↑ drospirenone possible	Clinical monitoring is recommended due to the potential for hyperkalemia. Consider using alternative ARV or contraceptive method.
Gender-Affirming Therapy	BIC, CAB (PO and IM), DTG, EVG/c, RAL	↔ goserelin, leuprolide acetate, and spironolactone expected	No dose adjustment needed.
	BIC, CAB (PO and IM), DTG, RAL	↔ estrogen expected	No dose adjustment needed.
		↔ testosterone expected	No dose adjustment needed.
	EVG/c	↑ estradiol possible ↑ cyproterone, dutasteride, and finasteride possible	Adjust dutasteride dose as needed based on clinical effects and endogenous hormone concentrations.
		↑ testosterone possible	Monitor masculinizing effects of testosterone and monitor for adverse effects. Adjust testosterone dose as necessary.
Menopausal Replacement Therapy	BIC, CAB (PO and IM), DTG, RAL	↔ estrogen expected with estradiol or conjugated estrogen (equine and synthetic) ↔ drospirenone, medroxyprogesterone, and micronized progesterone expected	No dose adjustment needed.
	EVG/c	↓ or ↑ estrogen possible ↑ drospirenone possible ↑ oral medroxyprogesterone possible	Adjust estrogen and progestin dose as needed based on clinical effects.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
		↑ oral micronized progesterone possible	
Immunosuppressants			
Cyclosporine, Everolimus, Sirolimus, Tacrolimus	BIC, CAB (PO and IM), DTG, RAL	↔ immunosuppressant expected	No dose adjustment needed.
	EVG/c	↑ immunosuppressant possible	Initiate with an adjusted dose of immunosuppressant to account for potential increased concentrations of the immunosuppressant. Monitor for immunosuppressant-related adverse events. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with a specialist as necessary.
Lipid-Modifying Agents			
Atorvastatin	BIC, CAB (PO and IM), DTG, RAL	↔ atorvastatin expected	No dose adjustment needed.
	EVG/c	Atorvastatin AUC ↑ 2.6-fold and C_{max} ↑ 2.3-fold	Titrate statin dose carefully. Administer the lowest effective dose while monitoring for adverse events. Do not exceed 20 mg atorvastatin daily.
Lomitapide	BIC, CAB (PO and IM), DTG, RAL	↔ lomitapide expected	No dose adjustment needed.
	EVG/c	↑ lomitapide expected	Contraindicated.
Lovastatin	BIC, CAB (PO and IM), DTG, RAL	↔ lovastatin expected	No dose adjustment needed.
	EVG/c	Significant ↑ lovastatin expected	Contraindicated.
Pitavastatin, Pravastatin	BIC, CAB (PO and IM), DTG, RAL	↔ statin expected	No dose adjustment needed.
	EVG/c	No data	No data available for dose recommendation.
Rosuvastatin	BIC, CAB (PO and IM), DTG, RAL	↔ rosuvastatin expected	No dose adjustment needed.
	EVG/c	Rosuvastatin AUC ↑ 38% and C_{max} ↑ 89%	Titrate statin dose carefully and use the lowest effective dose while monitoring for adverse events.
Simvastatin	BIC, CAB (PO and IM), DTG, RAL	↔ simvastatin expected	No dose adjustment needed.
	EVG/c	Significant ↑ simvastatin expected	Contraindicated.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Narcotics and Treatment for Opioid Dependence			
Buprenorphine Sublingual, buccal, or implant	BIC, CAB (PO and IM), DTG	↔ buprenorphine and norbuprenorphine (active metabolite) expected	No dose adjustment needed.
	EVG/c	Buprenorphine AUC ↑ 35% and C_{min} ↑ 66% Norbuprenorphine (active metabolite) AUC ↑ 42% and C_{min} ↑ 57%	No dose adjustment needed. Monitor for adverse events of buprenorphine. When transferring buprenorphine from transmucosal administration to implantation, monitor to ensure buprenorphine effect is adequate and not excessive.
	RAL	↔ buprenorphine and norbuprenorphine (active metabolite) (sublingual) ↔ buprenorphine or norbuprenorphine (active metabolite) expected (implant)	No dose adjustment needed.
Fentanyl	BIC, CAB (PO and IM), DTG, RAL	↔ fentanyl expected	No dose adjustment needed.
	EVG/c	↑ fentanyl	Monitor for fentanyl efficacy and adverse events, including potentially fatal respiratory depression.
Lofexidine	BIC, CAB (PO and IM), DTG, RAL	↔ lofexidine expected	No dose adjustment needed.
	EVG/c	↑ lofexidine possible	Monitor for lofexidine-related adverse events, including symptoms of orthostasis and bradycardia.
Methadone	All INSTIs	↔ methadone	No dose adjustment needed.
Tramadol	BIC, CAB (PO and IM), DTG, RAL	↔ tramadol and M1 (active metabolite) expected	No dose adjustment needed.
	EVG/c	↑ tramadol expected ↓ M1 (active metabolite) possible	Tramadol dose adjustments may be necessary. Monitor for clinical response and tramadol-related adverse events.
PDE5 Inhibitors			
Avanafil	BIC, CAB (PO and IM), DTG, RAL	↔ avanafil expected	No dose adjustment needed.
	EVG/c	No data	Do not coadminister.
Sildenafil	BIC, CAB (PO and IM), DTG, RAL	↔ sildenafil expected	No dose adjustment needed.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	EVG/c	↑ sildenafil expected	For Treatment of Erectile Dysfunction • Start with sildenafil 25 mg every 48 hours and monitor for adverse effects of sildenafil. Contraindicated for treatment of PAH.
Tadalafil	BIC, CAB (PO and IM), DTG, RAL	↔ tadalafil expected	No dose adjustment needed.
	EVG/c	↑ tadalafil expected	For Treatment of Erectile Dysfunction • Start with tadalafil 5 mg. 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. 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, CAB (PO and IM), DTG, RAL	↔ vardenafil expected	No dose adjustment needed.
	EVG/c	↑ vardenafil expected	Start with vardenafil 2.5 mg every 72 hours and monitor for adverse effects of vardenafil.
Sedative/Hypnotics			
Alprazolam, Clonazepam, Clorazepate, Diazepam, Estazolam, Flurazepam	BIC, CAB (PO and IM), DTG, RAL	↔ benzodiazepine expected	No dose adjustment needed.
	EVG/c	↑ benzodiazepine possible	Dose reduction of benzodiazepine may be necessary. Initiate with a low dose and monitor for benzodiazepine-related adverse events. Consider using an alternative benzodiazepine, such as lorazepam, oxazepam, or temazepam.
Midazolam, Triazolam	BIC, CAB (PO and IM), RAL	↔ benzodiazepine expected	No dose adjustment needed.
	DTG	With DTG 25 mg • ↔ midazolam AUC	No dose adjustment needed.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	EVG/c	↑ midazolam expected ↑ triazolam expected	Contraindicated. Do not coadminister triazolam or oral midazolam and EVG/c. Parenteral midazolam can be administered in a closely monitored setting. Consider dose reduction, especially if >1 dose is administered.
Suvorexant	BIC, CAB (PO and IM), DTG, RAL	↔ suvorexant expected	No dose adjustment needed.
	EVG/c	↑ suvorexant expected	Do not coadminister.
Zolpidem	BIC, CAB (PO and IM), DTG, RAL	↔ zolpidem expected	No dose adjustment needed.
	EVG/c	↑ zolpidem expected	Initiate zolpidem at a low dose. Dose reduction of zolpidem may be necessary.
Miscellaneous Drugs			
Calcifediol	BIC, CAB (PO and IM), DTG, RAL	↔ calcifediol expected	No dose adjustment needed.
	EVG/c	↑ calcifediol possible	Dose adjustment of calcifediol may be required. Monitor serum 25-hydroxyvitamin D, intact PTH, and serum Ca concentrations.
Cisapride	BIC, CAB (PO and IM), DTG, RAL	↔ cisapride expected	No dose adjustment needed.
	EVG/c	↑ cisapride expected	Contraindicated.
Colchicine	BIC, CAB (PO and IM), DTG, RAL	↔ colchicine expected	No dose adjustment needed.
	EVG/c	↑ colchicine expected	Do not coadminister in patients with hepatic or renal impairment. For Treatment of Gout Flares • Administer a single dose of colchicine 0.6 mg, followed by colchicine 0.3 mg 1 hour later. Do not repeat dose for at least 3 days. For Prophylaxis of Gout Flares • If original dose was colchicine 0.6 mg twice daily, decrease to colchicine 0.3 mg once daily. If dose was 0.6 mg once daily, decrease to 0.3 mg every other day.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
			For Treatment of Familial Mediterranean Fever • Do not exceed colchicine 0.6 mg once daily or 0.3 mg twice daily.
Dronabinol	BIC, CAB (PO and IM), DTG, RAL	↔ dronabinol expected	No dose adjustment needed.
	EVG/c	↑ dronabinol possible	Monitor for dronabinol-related adverse events.
Eluxadoline	BIC, CAB (PO and IM), DTG, RAL	↔ eluxadoline expected	No dose adjustment needed.
	EVG/c	↑ eluxadoline possible	Monitor for eluxadoline-related adverse events.
Ergot Derivatives	BIC, CAB (PO and IM), DTG, RAL	↔ dihydroergotamine, ergotamine, and methylergonovine expected	No dose adjustment needed.
	EVG/c	↑ dihydroergotamine, ergotamine, and methylergonovine expected	Contraindicated.
Flibanserin	BIC, CAB (PO and IM), DTG, RAL	↔ flibanserin expected	No dose adjustment needed.
	EVG/c	↑ flibanserin expected	Contraindicated.
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 administered simultaneously with Fe or Ca and food BIC AUC ↓ 33% if administered simultaneously with $CaCO_3$ under fasting conditions BIC AUC ↓ 63% if administered simultaneously with Fe under fasting conditions	With Supplements That Contain Ca or Fe • Administer BIC and supplements that contain Ca or Fe together with food. Do not coadminister BIC under fasting conditions simultaneously with, or 2 hours after, supplements that contain Ca or Fe.
	CAB	↓ INSTI possible	If coadministration is necessary, administer INSTI at least 2 hours before or at least 4 hours after supplements that contain polyvalent cations, including but not limited to the following products: cation-containing laxatives; Fe, Ca, or Mg supplements; and sucralfate. Monitor for virologic response. Many oral multivitamins also contain varying amounts of polyvalent cations; the extent and significance of chelation is unknown.
	DTG	DTG AUC ↓ 39% if administered simultaneously with $CaCO_3$ under fasting conditions	With Supplements That Contain Ca or Fe • Administer DTG and supplements that contain Ca or Fe together with food, or administer DTG at least 2 hours before or at least 6 hours after supplement.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
		DTG AUC ↓ 54% if administered simultaneously with Fe under fasting conditions ↔ DTG when administered with Ca or Fe supplement simultaneously with food	Do not coadminister DTG under fasting conditions simultaneously with, or 2 hours after, supplements that contain Ca or Fe.
	EVG/c, RAL	↓ INSTI possible	If coadministration is necessary, administer INSTI at least 2 hours before or at least 6 hours after supplements that contain polyvalent cations, including but not limited to the following products: cation-containing laxatives; Fe, Ca, or Mg supplements; and sucralfate. Monitor for virologic response. Many oral multivitamins also contain varying amounts of polyvalent cations; the extent and significance of chelation is unknown.

Key to Symbols

↑ = increase
↓ = decrease
↔ = no change

Key: Al = aluminum; ALT = alanine aminotransferase; ART = antiretroviral therapy; ARV = antiretroviral; AST = aspartate aminotransferase; AUC = area under the curve; BIC = bictegravir; Ca = calcium; CAB = cabotegravir; $CaCO_3$ = 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; ECG = electrocardiogram; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; Fe = iron; FTC = emtricitabine; GI = gastrointestinal; IM = intramuscular; INR= international normalized ratio; INSTI = integrase strand transfer inhibitor; Mg = magnesium; PAH = pulmonary arterial hypertension; PDE5 = phosphodiesterase type 5; PO = orally; PTH = parathyroid hormone; QTc = QT corrected for heart rate; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SSRI = selective serotonin reuptake inhibitors; TAF = tenofovir alafenamide; TCA = tricyclic antidepressants; TDF = tenofovir disoproxil fumarate; Zn = zinc

Table 24e. Drug Interactions between the CCR5 Antagonist Maraviroc and Other Drugs (Including Antiretroviral Agents)

In the table below, "no dose adjustment needed" indicates that the U.S. Food and Drug Administration–approved dose of maraviroc (MVC) 300 mg twice daily should be used. Recommendations for managing a particular drug interaction may differ, depending on whether a new antiretroviral (ARV) drug is being initiated in a patient on a stable concomitant medication or a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgement to select the most appropriate alternative medication to use.

Concomitant Drug Class/ Name	Effect on CCR5 Antagonist and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antibacterials—Macrolides		
Azithromycin	↔ MVC expected	No dose adjustment needed.
Clarithromycin	↑ MVC possible	MVC 150 mg twice daily
Erythromycin	↑ MVC possible	No dose adjustment needed.
Anticonvulsants		
Carbamazepine, Phenobarbital, Phenytoin	↓ MVC possible	If Used *without* a Strong CYP3A Inhibitor • MVC 600 mg twice daily If Used *with* a Strong CYP3A Inhibitor • MVC 150 mg twice daily
Eslicarbazepine	↓ MVC possible	Consider alternative ARV or anticonvulsant.
Oxcarbazepine	↓ MVC possible	Consider alternative ARV or anticonvulsant.
Antifungals		
Fluconazole	↑ MVC possible	No dose adjustment needed.
Isavuconazole	↑ MVC possible	No dose adjustment needed.
Itraconazole	↑ MVC possible	MVC 150 mg twice daily
Posaconazole	↑ MVC possible	MVC 150 mg twice daily
Voriconazole	↑ MVC possible	MVC 150 mg twice daily
Antimycobacterials		
Rifabutin	MVC AUC ↔ and C_{min} ↓ 30%	If Used *without* a Strong CYP3A Inhibitor • MVC 300 mg twice daily If Used *with* a Strong CYP3A Inhibitor • MVC 150 mg twice daily

Table 24e. Drug Interactions between the CCR5 Antagonist Maraviroc and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug Class/ Name	Effect on CCR5 Antagonist and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Rifampin	MVC AUC ↓ 63%	If Used *without* a Strong CYP3A Inhibitor • MVC 600 mg twice daily If Used *with* a Strong CYP3A Inhibitor • Consider alternative ARV or antimycobacterial.
Rifapentine	↓ MVC expected	Do not coadminister.
Antivirals - Orthopoxviruses (Smallpox, Mpox)		
Brincidofovir	↔ MVC expected	No dose adjustment needed.
Cidofovir	↔ MVC expected	No dose adjustment needed.
Tecovirimat	When Given with MVC without a Boosted PI or Other Potent CYP3A4 Inhibitors • ↓ MVC possible but not expected to be clinically relevant When Given with MVC Plus a Boosted PI or Other Potent CYP3A4 Inhibitors • ↑ MVC expected	If Used *without* a Strong CYP3A Inhibitor • No dose adjustment needed. If Used *with* a Strong CYP3A Inhibitor • MVC 150 mg twice daily
Hepatitis C Direct-Acting Antivirals		
Elbasvir/Grazoprevir	↔ MVC expected	No dose adjustment needed.
Ledipasvir/Sofosbuvir	↔ MVC expected	No dose adjustment needed.
Glecaprevir/Pibrentasvir	↔ MVC expected	No dose adjustment needed.
Simeprevir	↔ MVC expected	No dose adjustment needed.
Sofosbuvir	↔ MVC expected	No dose adjustment needed.
Sofosbuvir/Velpatasvir	↔ MVC expected	No dose adjustment needed.
Sofosbuvir/Velpatasvir/Voxilaprevir	↔ MVC expected	No dose adjustment needed.
Herbal Products		
St. John's Wort	↓ MVC expected	Do not coadminister.
Hormonal Therapies		
Hormonal Contraceptives	↔ ethinyl estradiol or levonorgestrel	No dose adjustment needed.
Menopausal Hormone Replacement Therapy	↔ MVC or hormone replacement therapies expected	No dose adjustment needed.
Gender-Affirming Hormone Therapies	↔ MVC or gender-affirming hormones expected	No dose adjustment needed.

Table 24e. Drug Interactions between the CCR5 Antagonist Maraviroc and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug Class/ Name	Effect on CCR5 Antagonist and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antiretroviral Drugs		
Attachment Inhibitor		
FTR[a]	MVC AUC ↑ 25% ↔ TMR[a]	No dose adjustment needed.
Capsid Inhibitor		
LEN (SQ and PO)	↑ MVC possible	No dose adjustment needed.
INSTIs		
BIC, CAB (IM and PO), DTG	↔ MVC expected	No dose adjustment needed.
EVG/c	↑ MVC possible	MVC 150 mg twice daily
RAL	MVC AUC ↓ 21% RAL AUC ↓ 37%	No dose adjustment needed.
NNRTIs		
DOR, RPV (IM and PO)	↔ MVC expected	No dose adjustment needed.
EFV	MVC AUC ↓ 45%	If Used *without* a Strong CYP3A Inhibitor • MVC 600 mg twice daily If Used *with* a Strong CYP3A Inhibitor • MVC 150 mg twice daily
ETR	MVC AUC ↓ 53%	If Used *without* a Strong CYP3A Inhibitor • MVC 600 mg twice daily If Used *with* a Strong CYP3A Inhibitor • MVC 150 mg twice daily
NVP	↔ MVC AUC	If Used *without* a Strong CYP3A Inhibitor • MVC 300 mg twice daily If Used *with* a Strong CYP3A Inhibitor • MVC 150 mg twice daily
PIs		
ATV Unboosted, ATV/c, ATV/r	With Unboosted ATV • MVC AUC ↑ 257% With (ATV/r 300 mg/100 mg) Once Daily • MVC AUC ↑ 388%	MVC 150 mg twice daily

Table 24e. Drug Interactions between the CCR5 Antagonist Maraviroc and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug Class/ Name	Effect on CCR5 Antagonist and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
DRV/c, DRV/r	With (DRV/r 600 mg/100 mg) Twice Daily • MVC AUC ↑ 305% With (DRV/r 600 mg/100 mg) Twice Daily and ETR • MVC AUC ↑ 210%	MVC 150 mg twice daily
LPV/r	MVC AUC ↑ 295% With LPV/r and EFV • MVC AUC ↑ 153%	MVC 150 mg twice daily

[a] FTR is a prodrug metabolized to its active moiety, TMR. Therefore, the effect on gp120-directed attachment inhibitor in the table refers to TMR concentrations.

Key to Symbols

↑ = increase
↓ = decrease
↔ = no change

Key: ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; CAB = cabotegravir; C_{min} = minimum plasma concentration; CYP = cytochrome P; DOR = doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FTR = fostemsavir; IM = intramuscular; INSTI = integrase strand transfer inhibitor; LEN = lenacapavir; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PO = orally; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQ = subcutaneous; TMR = temsavir

Table 24f. Drug Interactions between HIV-1 gp120-Directed Attachment Inhibitors and Other Drugs (Including Antiretroviral Agents)

Fostemsavir (FTR), an HIV-1 gp120-directed attachment inhibitor, is a prodrug of temsavir (TMR). In this table, the effect on gp120-directed attachment inhibitor refers to TMR concentrations. Recommendations for managing a particular drug interaction may differ depending on whether a new antiretroviral (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. Providers should exercise their clinical judgement to select the most appropriate alternative medication to use in cases where an interacting drug needs to be replaced with an alternative.

Concomitant Drug Class/ Name	Effect on gp120-Directed Attachment Inhibitor and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers		
H2 Receptor Antagonists	↔ TMR	No dose adjustment needed.
Anticonvulsants		
Carbamazepine, Phenobarbital, Phenytoin	↓ TMR expected	Contraindicated.
Antibacterials—Antimycobacterials		
Rifabutin	With Rifabutin 300 mg Once Daily and without RTV • TMR AUC ↓ 30% With Rifabutin 150 mg Once Daily and with RTV 100 mg Once Daily • TMR AUC ↑ 66%	If Used *without* PI/r • No dosage adjustment needed. If Used *with* PI/r • Recommended dose is rifabutin 150 mg once daily. • No dosage adjustment of FTR.
Rifampin	TMR AUC ↓ 72%	Contraindicated.
Rifapentine	↓ TMR expected	Do not coadminister.
Antivirals—Orthopoxviruses (Smallpox, Mpox)		
Brincidofovir	↑ brincidofovir possible	Give FTR dose at least 3 hours after administering brincidofovir, and monitor for brincidofovir-related adverse events (i.e., elevations in ALT/AST and bilirubin and GI adverse events).
Cidofovir	↔ TMR expected	No dose adjustment needed.
Tecovirimat	↔ TMR expected	No dose adjustment needed.
Hepatitis C Direct-Acting Antivirals		

Table 24f. Drug Interactions between HIV-1 gp120-Directed Attachment Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug Class/ Name	Effect on gp120-Directed Attachment Inhibitor and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Elbasvir/Grazoprevir	↑ grazoprevir expected	Increased grazoprevir exposures may increase the risk of ALT elevations. Use an alternative HCV regimen.
Ledipasvir/Sofosbuvir	↔ expected	No dose adjustment needed.
Glecaprevir/Pibrentasvir	↔ expected	No dose adjustment needed.
Sofosbuvir	↔ expected	No dose adjustment needed.
Sofosbuvir/Velpatasvir	↔ expected	No dose adjustment needed.
Sofosbuvir/Velpatasvir/Voxilaprevir	↑ voxilaprevir expected	Use an alternative HCV regimen if possible.
Herbal Products		
St. John's Wort	↓ TMR expected	Contraindicated.
Hormonal Therapies		
Contraceptives: Oral	ethinyl estradiol AUC ↑ 40% ↔ norethindrone	Prescribe oral contraceptive that contains no more than 30 mcg of ethinyl estradiol[a] or use alternative ARV or contraceptive methods.
Gender-Affirming Hormone Therapies	No data	No data available to make dose recommendation.
Menopausal Hormone Replacement Therapy	No data	No data available to make dose recommendation.
Lipid-Modifying Agents		
Atorvastatin, Fluvastatin, Pitavastatin, Simvastatin	↑ statin possible ↔ expected	Increased statin concentration may not be clinically relevant. Follow clinical guidelines. Administer the lowest effective statin dose while monitoring for adverse events.
Rosuvastatin	Rosuvastatin AUC ↑ 69%	Increased rosuvastatin concentration may not be clinically relevant. Follow clinical guidelines. Administer the lowest effective dose while monitoring for adverse events.
Narcotics and Treatment for Opioid Dependence		
Buprenorphine/Naloxone	Buprenorphine AUC ↑ 30% Norbuprenorphine (active metabolite) AUC ↑ 39%	No dose adjustment needed.

Table 24f. Drug Interactions between HIV-1 gp120-Directed Attachment Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug Class/ Name	Effect on gp120-Directed Attachment Inhibitor and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Methadone	↔ Total methadone ↔ R(−) methadone (active metabolite) ↔ S(+) methadone	No dose adjustment needed.
Antiretroviral Drugs		
Capsid Inhibitor		
LEN (SQ and PO)	↔ TMR expected ↔ LEN expected	No dose adjustment needed.
CCR5 Antagonist		
MVC	↔ TMR MVC AUC ↑ 25%	No dose adjustment needed.
CD4 Post Attachment Inhibitor		
IBA	↔ expected	No dose adjustment needed.
INSTIs		
BIC, CAB (IM and PO), DTG, EVG/c	↔ TMR expected	No dose adjustment needed.
RAL plus TDF	↔ TMR	No dose adjustment needed.
NRTIs		
TDF	↔ TMR ↔ TDF	No dose adjustment needed.
NNRTIs		
DOR, RPV (IM and PO)	↔ TMR expected	No dose adjustment needed.
EFV	↓ TMR possible ↔ EFV expected	No dose adjustment needed.

Table 24f. Drug Interactions between HIV-1 gp120-Directed Attachment Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug Class/ Name	Effect on gp120-Directed Attachment Inhibitor and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
ETR	TMR AUC ↓ 50% ↔ ETR	No dose adjustment needed.
ETR plus DRV/r	TMR C_{max} and AUC ↑ 34% to 53% ↔ DRV, RTV ETR AUC ↑ 28%	No dose adjustment needed.
PIs		
ATV Unboosted, ATV/c	↑ TMR possible ↔ ATV expected	No dose adjustment needed.
ATV/r	TMR C_{max} and AUC ↑ 54% to 58% ↔ ATV, RTV	No dose adjustment needed.
DRV/c	TMR C_{max} and AUC ↑ 79% to 97% ↔ DRV, RTV expected	No dose adjustment needed.
DRV/r	TMR C_{max} and AUC ↑ 52% to 63% ↔ DRV, RTV	No dose adjustment needed.
LPV/r	↑ TMR possible ↔ LPV expected	No dose adjustment needed.

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

Key to Symbols

↑ = increase
↓ = decrease
↔ = no change

Key: ALT = alanine aminotransferase; ARV = antiretroviral; AST = aspartate aminotransferase; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; C_{max} = maximum plasma concentration; CAB = cabotegravir; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FTR = fostemsavir; GI = gastrointestinal; HCV = hepatitis C virus; IBA = ibalizumab; IM = intramuscular; INSTI = integrase strand transfer inhibitor; LEN = lenacapavir; LPV = lopinavir; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PI/r = ritonavir-boosted PI; PO = orally; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQ = subcutaneous; TDF = tenofovir disoproxil

Table 24f. Drug Interactions between HIV-1 gp120-Directed Attachment Inhibitors and Other Drugs (Including Antiretroviral Agents)

fumarate; TMR = temsavir

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

This table provides information on the known or predicted interactions between lenacapavir (LEN), an HIV capsid inhibitor, and other drugs, including antiretroviral (ARV) drugs.

LEN is available as an oral tablet (to be used only as initial therapy) and a long-acting injectable formulation that is administered every 6 months. LEN is a moderate cytochrome P450 (CYP) 3A4 inhibitor and may increase the concentration of drugs metabolized by CYP3A4. Due to the long half-life of the injectable formulation, this inhibitory effect may persist, and clinicians should continue to assess for drug interactions for up to 9 months after the last LEN injection. Recommendations for managing a particular drug interaction may differ depending on whether LEN is being initiated in a patient on a stable concomitant medication or whether a new medication is being initiated in a patient on a stable LEN-containing ARV regimen.

The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. Providers should exercise their clinical judgement to select the most appropriate alternative medication to use in cases where an interacting drug needs to be replaced with an alternative. People with HIV should be counseled about the importance of informing all their health care providers about their HIV regimen prior to starting any new concomitant medications (e.g., prescription, over the counter, and herbs or dietary supplements) to minimize the risk of drug–drug interactions.

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia		
Alfuzosin	↑ alfuzosin expected	Consider an alternative to alfuzosin or an alternative ARV. If coadministered, monitor blood pressure.
Doxazosin	↑ doxazosin possible	No dose adjustment needed. Monitor blood pressure.
Tamsulosin	↑ tamsulosin possible	No dose adjustment needed. Monitor blood pressure.
Terazosin	↔ terazosin expected	No dose adjustment needed.
Silodosin	↑ silodosin possible	No dose adjustment needed.
Antibacterials—Antimycobacterials		
Bedaquiline	↑ bedaquiline possible	Consider alternatives unless benefits outweigh risks. Monitor liver function and ECG for QTc prolongation.
Rifabutin	↓ LEN expected	Do not coadminister.
Rifampin	LEN AUC ↓84%	Contraindicated.
Rifapentine	↓ LEN expected	Do not coadminister.
Antibacterials—Macrolides		
Azithromycin	↔ LEN expected	No dose adjustment needed.
Clarithromycin	↑ LEN possible	No dose adjustment needed.
Erythromycin	↑ LEN possible	No dose adjustment needed.

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Anticoagulants		
Apixaban	↑ apixaban possible	No dose adjustment needed. Monitor for apixaban-related adverse events, such as increased bleeding.
Dabigatran	↑ dabigatran possible	No dose adjustment needed. Monitor for dabigatran-related adverse events, such as increased bleeding.
Edoxaban	↑ edoxaban possible	No dose adjustment needed. Monitor for edoxaban-related adverse events, such as increased bleeding.
Rivaroxaban	↑ rivaroxaban possible	Monitor for rivaroxaban-related adverse events, such as increased bleeding, and adjust rivaroxaban dose accordingly.
Warfarin	↑ warfarin possible	Monitor INR and adjust warfarin dose accordingly.
Anticonvulsants		
Carbamazepine	↓ LEN expected	Contraindicated.
Eslicarbazepine	↓ LEN expected	Do not coadminister. Consider alternative anticonvulsant or ARV.
Ethosuximide	↑ ethosuximide possible	Monitor for ethosuximide-related adverse events and adjust ethosuximide dose accordingly.
Lamotrigine	↔ expected	No dose adjustment needed.
Oxcarbazepine	↓ LEN expected	Do not coadminister. Consider alternative anticonvulsant or ARV.
Phenobarbital	↓ LEN expected	Do not coadminister. Consider alternative anticonvulsant or ARV.
Phenytoin	↓ LEN expected	Contraindicated.
Valproic Acid	↔ expected	No dose adjustment needed.
Antidepressants, Anxiolytics, and Antipsychotics Also see the Sedative/Hypnotics section below.		
Bupropion	↔ expected	No dose adjustment needed.
Buspirone	↑ buspirone expected	Administer lowest dose of buspirone with caution and titrate buspirone dose based on clinical response. Dose reduction may be necessary. Monitor for buspirone-related adverse events.
Nefazodone	↑ LEN possible	No dose adjustment needed.

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Trazodone	↑ trazodone expected	Administer lowest dose of trazodone and monitor for CNS and CV adverse events.
Tricyclic Antidepressants Amitriptyline, amoxapine, clomipramine, desipramine, doxepin, imipramine, maprotiline, nortriptyline, protriptyline, trimipramine	↔ expected	No dose adjustment needed.
Selective Serotonin Reuptake Inhibitor Paroxetine	↑ paroxetine possible	Dose reduction may be necessary. Monitor for paroxetine-related adverse events.
Selective Serotonin Reuptake Inhibitors (e.g., citalopram, escitalopram, fluoxetine, fluvoxamine, sertraline)	↔ expected	No dose adjustment needed.
Antipsychotics		
Aripiprazole	↑ aripiprazole possible	No dose adjustment needed.
Brexpiprazole	↑ aripiprazole expected	If patient is known CYP2D6 poor metabolizer, then administer quarter of usual brexpiprazole dose.
Cariprazine	↑ cariprazine possible	No dose adjustment needed.
Iloperidone	↑ iloperidone possible	No dose adjustment needed or consider dose reduction. Monitor for iloperidone-related adverse events.
Lumateperone	↑ lumateperone expected	Recommended dose of lumateperone is 21 mg once daily.
Lurasidone	↑ lurasidone expected	If LEN is added to lurasidone therapy, administer half of lurasidone dose. If lurasidone is added to LEN therapy, the recommended starting dose of lurasidone is 20 mg daily, and the maximum recommended dose is 80 mg daily.
Olanzapine	↔ expected	No dose adjustment needed.
Pimavanserin	↑ pimavanserin possible	No dose adjustment needed. Monitor ECG for QTc prolongation.
Pimozide	↑ pimozide expected	Do not coadminister.
Quetiapine	↑ quetiapine expected	Consider alternatives unless benefits outweigh risks. Monitor ECG for QTc prolongation and consider dose reduction accordingly.
Ziprasidone	↔ expected	No dose adjustment needed.
Antifungals		
Fluconazole	↔ expected	No dose adjustment needed.

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Isavuconazole	↔ expected	No dose adjustment needed.
Itraconazole	↑ LEN possible	No dose adjustment needed.
Posaconazole	↑ LEN possible	No dose adjustment needed.
Voriconazole	↑ LEN AUC 41%	No dose adjustment needed.
Antimalarials		
Artemether/Lumefantrine	↑ artemether and lumefantrine possible	Monitor for lumefantrine-related adverse events, including QTc prolongation.
Atovaquone/Proguanil	↔ expected	No dose adjustment needed.
Mefloquine	↑ mefloquine possible	Monitor for mefloquine-related adverse events, including QTc prolongation.
Antiplatelets		
Clopidogrel	↓ clopidogrel active metabolite possible	Consider alternative ARV or antiplatelet drug. If coadministered, monitor for clopidogrel-related adverse events.
Prasurgrel	↔ expected	No dose adjustment needed.
Ticagrelor	↑ ticagrelor possible	No dose adjustment needed. Monitor for ticagrelor-related adverse events.
Vorapaxar	↑ vorapaxar possible	No dose adjustment needed.
Antiretroviral Drugs		
CCR5 Antagonist		
MVC	↔ expected	No dose adjustment needed.
CD4 Post Attachment Inhibitor		
IBA	↔ expected	No dose adjustment needed.
gp120 Attachment Inhibitor		
FTR	↔ expected	No dose adjustment needed.
INSTIs		
BIC, CAB (IM or PO), DTG, EVG/c, RAL	↔ expected	No dose adjustment needed.
NRTIs		
ABC, 3TC, FTC	↔ expected	No dose adjustment needed.
TAF	TAF AUC ↑ 32%	No dose adjustment needed.
TDF	TDF AUC ↑ 47%	No dose adjustment needed.
NNRTIs		
EFV	LEN AUC↓ 56%	Do not coadminister.
ETR	↓ LEN expected	Do not coadminister.

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
DOR	↑ DOR possible	No dose adjustment needed.
NVP	↓ LEN expected	Do not coadminister.
RPV (IM or PO)	↑ RPV possible	No dose adjustment needed.
PIs		
ATV unboosted, ATV/r	↑ LEN expected	Do not coadminister.
ATV/c	LEN AUC ↑ 4-fold	Do not coadminister.
DRV/c	DRV/c AUC ↑ 94%	No dose adjustment needed.
DRV/r	↑ LEN expected	No dose adjustment needed.
LPV/r	↑ LEN expected	No dose adjustment needed.
Antivirals—Orthopoxviruses (Mpox, Smallpox)		
Brincidofovir	↔ expected	No dose adjustment needed.
Cidofovir	↔ expected	No dose adjustment needed.
Tecovirimat	↓ LEN possible	No dose adjustment needed.
Beta-Agonists, Long-Acting Inhaled		
Arformoterol, Formoterol, Indacaterol, Olodaterol, Salmeterol	↔ expected	No dose adjustment needed.
Cardiac Medications		
Amiodarone	↑ amiodarone expected ↑ LEN possible	Do not coadminister.
Disopyramide	↑ disopyramide expected	Do not coadminister.
Lidocaine, Propafenone	↑ lidocaine possible ↑ propafenone possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor for antiarrhythmic-related adverse events and monitor concentrations, if available.
Dofetilide, Fecainide, Mexiletine	↔ expected	No dose adjustment needed.
Dronedarone	↑ dronedarone possible ↑ LEN possible	Consider alternative ARV or cardiac medication. If coadminstered, monitor for dronedarone-related adverse events.
Quinidine	↑ quinidine expected	Do not coadminster.
Beta Blockers (e.g., carvediol, metoprolol, timolol)	↔ expected	No dose adjustment needed.
Bosentan	↓ LEN expected	Do not coadminister.
Calcium Channel Blockers		
Diltiazem, Verapamil	↑ diltiazem and verapamil possible	Monitor and dose adjust according to clinical response and adverse events.

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Digoxin	↑ digoxin expected	Consider alternative ARV or antiarrhythmic. If coadministered, monitor digoxin therapeutic concentration.
Eplerenone	↑ eplerenone expected	For Post-MI CHF • Dosing of eplerenone should not exceed 25 mg daily. For Hypertension • Initiate at 25 mg once daily. Dosing may be increased to a maximum of 25 mg twice daily.
Ranolazine	↑ ranolazine expected	Limit ranolazine to 500 mg twice daily.
Ivabradine	↑ ivabradine expected	Do not coadminister.
Corticosteroids		
Beclomethasone Inhaled or intranasal Ciclesonide Inhaled	↔ expected	No dose adjustment needed.
Budesonide, Fluticasone, Mometasone Inhaled or intranasal	↑ budesonide, fluticasone, mometasone possible	Initiate with the lowest starting dose and titrate carefully and monitor for adrenal insufficiency, Cushing's syndrome, and other corticosteroid-related adverse events.
Betamethasone Systemic	↔ expected	No dose adjustment needed.
Budesonide, Prednisone, Prednisolone Systemic	↑ glucocorticoids expected	Initiate with the lowest starting dose, titrate carefully, and monitor for adrenal insufficiency, Cushing's syndrome, and other corticosteroid-related adverse events.
Dexamethasone Systemic	↑ dexamethasone expected ↓ LEN expected if used with dexamethasone >16 mg/day	Initiate with the lowest starting dose, titrate carefully, and monitor for adrenal insufficiency, Cushing's syndrome, and other corticosteroid-related adverse events. Do not coadminister with dexamethasone >16 mg/day.
Betamethasone, Methylprednisoline, Triamicinolone Local injections, including intra-articular, epidural, or intra-orbital	↑ glucocorticoids possible	Monitor for adrenal insufficiency, Cushing's syndrome, and other corticosteroid-related adverse events.
Glucose-Lowering Medications		
Canagliflozin	↔ expected	No dose adjustment needed.

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Saxagliptin	↑ saxagliptin possible	No dose adjustment needed.
Dapagliflozin/Saxagliptin	↑ saxagliptin possible	No dose adjustment needed.
Hepatitis C Direct-Acting Antiviral Agents		
Elbasvir/Grazoprevir	↔ expected	No dose adjustment needed.
Glecaprevir/Pibrentasvir	↔ expected	No dose adjustment needed.
Ledipasvir/Sofosbuvir	↔ expected	No dose adjustment needed.
Sofosbuvir/Velpatasvir	↔ expected	No dose adjustment needed.
Sofosbuvir/Velpatasvir/Voxilaprevir	↔ expected	No dose adjustment needed.
Herbal Products		
St. John's Wort	↓ LEN expected	Contraindicated.
Hormonal Therapies		
Contraceptives—Injectable Depot MPA	↑ MPA possible	No dose adjustment needed.
Contraceptives—Oral Drosperinone, Ethinyl Estradiol, Levonorgestrel, Norethindrone, Norgestimate Subdermal Implant Etonogstrel Subdermal Implant Levonorgestrel Transdermal Ethinyl Estradiol/Norelgestromin Vaginal Ring Etonogestrel/Ethinyl Estradiol Vaginal Ring Segesterone/Ethinyl Estradiol	↑ contraceptive exposures possible	No dose adjustment needed.
Emergency Contraceptives Levonorgestrel (oral)	↑ levonorgestrel possible	No dose adjustment needed.
Gender-Affirming Therapy		
Estradiol, Goserelin, Leuprolide Acetate, Finasteride	↔ expected	No dose adjustment needed.
Dutasteride, Testosterone	↑ dutasteride and testosterone possible	No dose adjustment needed.
Menopausal Hormone Replacement Therapy		
Conjugated Estrogen (equine and synthetic), Micronized	↑ estrogen and progesterone possible	No dose adjustment needed.

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Progesterone, Medroxyprogesterone		
Drospirenone	↑ drospirenone possible	No dose adjustment needed.
Immunosuppressants		
Cyclosporine, Everolimus, Sirolimus, Tacrolimus	↑ immunosuppressant expected	Initiate with an adjusted dose of immunosuppressant to account for potential increased concentrations of the immunosuppressant and monitor for immunosuppressant-related adverse events. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with a specialist as necessary.
Lipid-Modifying Agents		
Atorvastatin	↑ atorvastatin possible	No dose adjustment needed.
Lomitapide	↑ lomitapide expected	Contraindicated.
Lovastatin	↑ lovastatin expected	Administer the lowest effective lovastatin dose while monitoring for adverse events
Pitavastatin	↔ expected	No dose adjustment needed.
Pravastatin	↔ expected	No dose adjustment needed.
Rosuvastatin	↑ rosuvastatin possible	No dose adjustment needed.
Simvastatin	↑ simvastatin expected	Administer the lowest effective simvastatin dose while monitoring for adverse events.
Narcotics and Treatment for Opioid Dependence		
Buprenorphine Sublingual, buccal, or implant	↑ buprenorphine possible	Initiation of Buprenorphine in Patients Taking LEN • Titrate buprenorphine dose to desired effect and use the lowest feasible initial dose. Initiation of LEN in Patients Taking Buprenorphine • Dose adjustment for buprenorphine may be needed. Monitor for buprenorphine-related adverse events.
Fentanyl	↑ fentanyl possible	Monitor for fentanyl-related adverse events, including potentially fatal respiratory depression. Fentanyl dose reduction may be necessary.
Lofexidine	↔ expected	No dose adjustment needed.
Methadone	↑ methadone possible	No dose adjustment needed.

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Oxycodone	↑ oxycodone possible	Monitor for opioid-related adverse events, including potentially fatal respiratory depression. Oxycodone dose reduction may be necessary.
Tramadol	↑ tramadol possible	Tramadol dose adjustments may be necessary. Monitor for clinical response and tramadol-related adverse events.
PDE5 Inhibitors		
Avanafil	↑ avanafil expected	Avanafil dose should not exceed 50 mg once every 24 hours.
Sildenafil	↑ sildenafil expected	For Treatment of Erectile Dysfunction • Start with sildenafil 25 mg and monitor for sildenafil-related adverse events. For Treatment of PAH • Reduce the dose of sildenafil to 20 mg three times a day when discontinuing treatment with LEN.
Tadalafil	↑ tadalafil expected	No dose adjustment needed.
Vardenafil	↑ vardenafil expected	Vardenafil dose should not exceed 5 mg once every 24 hours.
Sedative/Hypnotics		
Alprazolam	↑ alprazolam expected	Consider lowest dose and monitor for alprazolam-related adverse events.
Clonazepam	↑ clonazepam possible	Consider alternative benzodiazepines.
Diazepam	↑ diazepam possible	Consider lowest dose and monitor for benzodiazepine-related events.
Lorazepam, Oxazepam, Temazepam	↔ expected	No dose adjustment needed.
Midazolam (Oral)	↑ midazolam expected	Use with caution and consider alternative benzodiazepine.
Suvorexant	↑ midazolam expected	Initiate suvorexant dose at 5 mg daily. Suvorexant dose can be increased to 10 mg once per night if the 5 mg dose is not effective.
Triazolam	↑ triazolam expected	Use with caution and consider alternative benzodiazepine.
Zolpidem	↑ zolpidem possible	Consider initiating zolpidem at a low dose.
Miscellaneous Drugs		
Cisapride	↑ cisapride expected	Do not coadminister.

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Colchicine	↑ colchicine expected	For Treatment of Gout Flares • Administer single colchicine dose of 1.2 mg. Do not repeat dose for at least 3 days. For Treatment of Familial Mediterranean Fever • Colchicine dose should not exceed 1.2 mg daily (may be given as 0.6 mg twice a day).
Ergot Derivatives Dihydroergotamine, ergotamine, methylergonovine	↑ dihydroergotamine, ergotamine, methylergonovine expected	Do not coadminister.
Flibanserin	↑ flibanserin expected	Do not coadminister.
Naloxegol	↑ naloxegol expected	Avoid use; if coadministration is necessary, decrease dosage of naloxegol and monitor for naloxegol-related adverse events.

Key to Symbols

↑ = increase
↓ = decrease
↔ = no change

Key: 3TC = lamivudine; ABC = abacavir; AUC = area under the curve; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; CAB = cabotegravir; CHF = congestive heart failure; CNS = central nervous system; CV = cardiovascular; CYP = cytochrome P 450; DOR = doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; ECG = electrocardiogram; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; FTR = fostemsavir; IBA = ibalizumab; IM = intramuscular; INR = international normalized ratio; INSTI = integrase strand transfer inhibitor; QTc = QT corrected for heart rate; LEN = lenacapavir; LPV/r = lopinavir/ritonavir; MI = myocardial infarction; MPA = medroxyprogesterone acetate; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PAH = pulmonary arterial hypertension; PDE5 = phosphodiesterase type 5; PI = protease inhibitor; PO = orally; RAL = raltegravir; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Table 25a. Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors

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

Rilpivirine (RPV) intramuscular (IM) is not included in this table, because the combination of cabotegravir IM plus RPV IM is a two-drug co-packaged product. Therefore, RPV IM is not expected to be used as a protease inhibitor.

PIs		NNRTIs				
		DOR	EFV	ETR	NVP	RPV
ATV Unboosted	PK Data	↑ DOR expected ↔ ATV expected	↔ EFV ATV AUC ↓ 74%	ETR AUC ↑ 50% and C_{min} ↑ 58% ↔ ATV AUC and C_{min} ↓ 47%	↑ NVP possible ↓ ATV possible	↑ RPV PO possible ↔ ATV expected
	Dose	No dose adjustment needed.	Do not coadminister.	Do not coadminister.	Do not coadminister.	No dose adjustment needed.
ATV/c	PK Data	↑ DOR expected ↔ ATV expected	↔ EFV expected ↓ ATV possible ↓ COBI possible	↑ ETR possible ↓ ATV possible ↓ COBI possible	↑ NVP possible ↓ ATV possible ↓ COBI possible	↑ RPV PO possible ↔ ATV expected
	Dose	No dose adjustment needed.	ATV/c in ART-Naive Patients • ATV 400 mg plus COBI 150 mg once daily • Do not use coformulated ATV 300 mg/ COBI 150 mg. ATV/c in ART-Experienced Patients • Do not coadminister. No dose adjustment needed for EFV.	Do not coadminister.	Do not coadminister.	No dose adjustment needed.
ATV/r	PK Data	↑ DOR expected ↔ ATV expected	↔ EFV expected (ATV 400 mg plus RTV 100 mg) Once Daily	(ATV 300 mg plus RTV 100 mg) Once Daily • ETR AUC and C_{min} both ↑ ~30%	(ATV 300 mg plus RTV 100 mg) Once Daily	↑ RPV PO possible ↔ ATV expected

Table 25a. Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors

PIs		NNRTIs				
		DOR	EFV	ETR	NVP	RPV
			• ATV concentrations similar to (ATV 300 mg plus RTV 100 mg) without EFV	• ↔ ATV AUC and C_{min}	• ATV AUC ↓ 42% and C_{min} ↓ 72% • NVP AUC ↑ 25%	
	Dose	No dose adjustment needed.	ATV/r in ART-Naive Patients • (ATV 400 mg plus RTV 100 mg) once daily ATV/r in ART-Experienced Patients: • Do not coadminister. No dose adjustment needed for EFV.	No dose adjustment needed.	Do not coadminister.	No dose adjustment needed.
DRV/c	PK Data	↑ DOR expected ↔ DRV expected	↔ EFV 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%	↑ NVP possible ↓ DRV possible ↓ COBI possible	↔ DRV expected ↑ RPV PO possible
	Dose	No dose adjustment needed.	Do not coadminister.	Do not coadminister.	Do not coadminister.	No dose adjustment needed.
DRV/r	PK Data	↑ DOR expected ↔ DRV expected	With (DRV 300 mg plus RTV 100 mg) Twice Daily • EFV AUC ↑ 21% • ↔ DRV AUC and C_{min} ↓ 31%	ETR 100 mg Twice Daily with (DRV 600 mg plus RTV 100 mg) Twice Daily • ETR AUC ↓ 37% and C_{min} ↓ 49% • ↔ DRV	With (DRV 400 mg plus RTV 100 mg) Twice Daily • NVP AUC ↑ 27% and C_{min} ↑ 47% • DRV AUC ↑ 24%[a]	RPV 150 mg PO Once Daily with (DRV 800 mg plus RTV 100 mg) Once Daily • RPV PO AUC ↑ 130% and C_{min} ↑ 178% • ↔ DRV
	Dose	No dose adjustment needed.	Clinical significance unknown. Use standard doses and monitor patient closely. Consider monitoring drug levels.	No dose adjustment needed. Despite reduced ETR concentration, safety and efficacy of this combination	No dose adjustment needed.	No dose adjustment needed.

Table 25a. Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors

PIs		NNRTIs				
		DOR	EFV	ETR	NVP	RPV
				have been established in a clinical trial.		
LPV/r	PK Data	↑ DOR expected ↔ LPV expected	↔ EFV expected With LPV/r 500 mg/125 mg[b] Twice Daily • LPV concentration similar to that of LPV/r 400 mg/100 mg twice daily without EFV	ETR AUC ↓ 35% (comparable to the decrease seen with DRV/r) ↔ LPV AUC	↑ NVP possible LPV AUC ↓ 27% and C_{min} ↓ 51%	RPV 150 mg PO Once Daily with LPV/r • RPV PO AUC ↑ 52% and C_{min} ↑ 74% • ↔ LPV
	Dose	No dose adjustment needed.	LPV/r 500 mg/ 125 mg[a] twice daily LPV/r 533 mg/ 133 mg twice daily when using oral solution No dose adjustment needed for EFV.	No dose adjustment needed.	LPV/r 500 mg/ 125 mg[a] twice daily LPV/r 533 mg/133 mg twice daily when using oral solution No dose adjustment needed for NVP.	No dose adjustment needed.

[a] 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: ART = antiretroviral therapy; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; C_{min} = minimum plasma concentration; COBI = cobicistat; DLV = delavirdine; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; EFV = efavirenz; ETR = etravirine; FPV = fosamprenavir; IDV = indinavir; IM = intramuscular; LPV = lopinavir; LPV/r = lopinavir/ritonavir; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PO = oral; PK = pharmacokinetic; RPV = rilpivirine; RTV = ritonavir; SQV = saquinavir; TPV = tipranavir

Table 25b. Interactions Between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors

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

Information on drug interactions with oral (PO) cabotegravir (CAB) is not included in this table. The CAB PO tablet is not available in retail pharmacies and will be provided directly to patients for short-term use only (PO lead-in and to bridge intramuscular [IM] administration is delayed).

CAB IM and rilpivirine (RPV) IM also are not included in this table because the combination is a two-drug co-packaged product. Therefore, it is not anticipated that they will be used with oral NNRTIs or PIs.

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
NNRTIs					
DOR	PK Data	↔ DOR and BIC expected	↔ DOR DTG AUC ↑ 36% and C_{min} ↑ 27%	↑ DOR expected ↔ EVG	↔ DOR and RAL expected
	Dose	No dose adjustment needed.	No dose adjustment needed.	No dose adjustment needed.	No dose adjustment needed.
EFV	PK Data	↓ BIC expected	With DTG 50 mg Once Daily • DTG AUC ↓ 57% and C_{min} ↓ 75%	↑ or ↓ EVG, COBI, and EFV possible	With RAL 400 mg Twice Daily • RAL AUC ↓ 36% and C_{min} ↓ 21% With RAL 1,200 mg Once Daily • ↔ RAL AUC and C_{min}
	Dose	Do not coadminister.	In Patients Without INSTI Resistance • DTG 50 mg twice daily In Patients with Certain INSTI-Associated Resistance[a] or Clinically Suspected INSTI Resistance • Consider alternative combination.	Do not coadminister.	No dose adjustment needed.

Table 25b. Interactions Between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
ETR	PK Data	↓ BIC expected	ETR 200 mg Twice Daily plus DTG 50 mg Once Daily • DTG AUC ↓ 71% and C_{min} ↓ 88% ETR 200 mg Twice Daily with (DRV 600 mg plus RTV 100 mg) Twice Daily and DTG 50 mg Once Daily • DTG AUC ↓ 25% and C_{min} ↓ 37% ETR 200 mg Twice Daily with (LPV 400 mg plus RTV 100 mg) Twice Daily and DTG 50 mg Once Daily • DTG AUC ↑ 11% and C_{min} ↑ 28%	↑ or ↓ EVG, COBI, and ETR possible	ETR 200 mg Twice Daily plus RAL 400 mg Twice Daily • ETR C_{min} ↑ 17% • RAL C_{min} ↓ 34%
	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 Resistance[a] or Clinically Suspected INSTI Resistance • DTG 50 mg twice daily with ETR (concurrently with ATV/r, DRV/r, or LPV/r)	Do not coadminister.	RAL 400 mg twice daily Coadministration with RAL 1,200 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, and NVP possible	No data
	Dose	Do not coadminister.	No dose adjustment needed.	Do not coadminister.	No dose adjustment needed.

Table 25b. Interactions Between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
RPV	PK Data	No data	With DTG 50 mg Once Daily • ↔ DTG AUC and C_{min} ↑ 22% • ↔ RPV PO AUC and C_{min} ↑ 21%	↑ or ↓ EVG, COBI, and RPV PO possible	↔ RPV PO RAL C_{min} ↑ 27%
	Dose	No dose adjustment needed.	No dose adjustment needed.	Do not coadminister.	No dose adjustment needed.
PIs					
ATV	PK Data	ATV 400 mg Once Daily plus BIC 75 mg Single Dose • BIC AUC ↑ 315%	(ATV 400 mg plus DTG 30 mg) Once Daily • DTG AUC ↑ 91% and C_{min} ↑ 180%	↑ or ↓ EVG, COBI, and ATV possible	With Unboosted ATV • RAL AUC ↑ 72% With Unboosted ATV and RAL 1,200 mg • RAL AUC ↑ 67%
	Dose	Do not coadminister.	No dose adjustment needed.	Do not coadminister.	No dose adjustment needed.
ATV/c	PK Data	BIC AUC ↑ 306%	No data	Not applicable	No data
	Dose	Do not coadminister.	No dose adjustment needed.	Do not coadminister two COBI-containing products.	No dose adjustment needed.
ATV/r	PK Data	↑ BIC expected	(ATV 300 mg plus RTV 100 mg) Once Daily plus DTG 30 mg Once Daily • DTG AUC ↑ 62% and C_{min} ↑ 121%	Not applicable	With (ATV 300 mg plus RTV 100 mg) Once Daily • RAL AUC ↑ 41%
	Dose	Do not coadminister.	No dose adjustment needed.	Do not coadminister RTV and COBI.	No dose adjustment needed.
DRV	PK Data	Not applicable	Not applicable	↔ DRV or EVG expected	Not applicable
	Dose	Do not administer DRV without RTV or COBI.	Do not administer DRV without RTV or COBI.	No dose adjustment needed.	Do not administer DRV without RTV or COBI.

Table 25b. Interactions Between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
DRV/c	PK Data	BIC AUC ↑ 74%	DRV/c plus DTG Once Daily • ↔ DTG, DRV, and COBI DTG 50 mg Once Daily and DRV/r Once Daily Switched to DRV/c • DTG C_{min} ↑ 100%	Not applicable	No data
	Dose	No dose adjustment needed.	No dose adjustment needed.	Do not coadminister two COBI-containing products.	No dose adjustment needed.
DRV/r	PK Data	No data	(DRV 600 mg plus RTV 100 mg) Twice Daily with DTG 30 mg Once Daily • DTG AUC ↓ 22% and C_{min} ↓ 38%	Not applicable	With (DRV 600 mg plus RTV 100 mg) Twice Daily • RAL AUC ↓ 29% and C_{min} ↑ 38%
	Dose	No dose adjustment needed.	No dose adjustment needed.	Do not coadminister RTV and COBI.	No dose adjustment needed.
LPV/r	PK Data	No data	With (LPV 400 mg plus RTV 100 mg) Twice Daily and DTG 30 mg Once Daily • ↔ DTG	Not applicable	↓ RAL ↔ LPV/r
	Dose	Consider alternative combination.	No dose adjustment needed.	Do not coadminister RTV and COBI.	No dose adjustment needed.

[a] Refer to DTG product label for details.

Key to Symbols

↑ = increase
↓ = decrease
↔ = no change

Key: ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; C_{min} = minimum plasma concentration; CAB = cabotegravir; COBI = cobicistat; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; IM = intramuscular; INSTI = integrase strand transfer inhibitor; LPV = lopinavir; LPV/r = lopinavir/ritonavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PK = pharmacokinetic; PO = oral; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir

Appendix B, Table 1. Coformulated and Copackaged Antiretroviral Regimens

Updated: May 26, 2023
Reviewed: May 26, 2023

The following table includes dose recommendations for U.S. Food and Drug Administration (FDA)–approved coformulated and copackaged antiretroviral regimens for adults with HIV. Not all products are FDA-approved for adolescents with HIV. For information regarding the use of these medications in adolescents with HIV, including weight limitations and additional dosage forms, please consult FDA product labeling or the Pediatric Antiretroviral Guidelines. Please see the class-specific drug characteristics tables (Appendix B, Tables 3, 4, 5, and 6) for details about the individual drugs included in these products, including information on elimination and metabolic pathways, serum and intracellular half-lives, and adverse effects. The products in this table are listed by drug class and arranged **in alphabetical order** by trade name within each class.

Trade Name (Abbreviation)	ARV Drugs Included in the Regimen	Dosing Recommendation[a]
INSTI plus Two NRTIs		
Biktarvy (BIC/TAF/FTC)	Bictegravir 50 mg/tenofovir alafenamide 25 mg/emtricitabine 200 mg	One tablet PO once daily
Genvoya (EVG/c/TAF/FTC)	Elvitegravir 150 mg/cobicistat 150 mg/tenofovir alafenamide 10 mg/ emtricitabine 200 mg	One tablet PO 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 PO once daily with food
Triumeq (DTG/ABC/3TC)	Dolutegravir 50 mg/abacavir 600 mg/lamivudine 300 mg	One tablet PO once daily
INSTI plus One NRTI		
Dovato (DTG/3TC)	Dolutegravir 50 mg/lamivudine 300 mg	One tablet PO 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 PO 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 PO 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 PO once daily with food

Appendix B, Table 1. Coformulated and Copackaged Antiretroviral Regimens

Trade Name (Abbreviation)	ARV Drugs Included in the Regimen	Dosing Recommendation[a]
Delstrigo (DOR/TDF/3TC)	Doravirine 100 mg/tenofovir disoproxil fumarate 300 mg/lamivudine 300 mg	One tablet PO once daily
Odefsey (RPV/TAF/FTC)	Rilpivirine 25 mg/tenofovir alafenamide 25 mg/emtricitabine 200 mg	One tablet PO once daily with food
Symfi (EFV/TDF/3TC)	Efavirenz 600 mg/tenofovir disoproxil fumarate 300 mg/lamivudine 300 mg	One tablet PO 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 PO once daily on an empty stomach, preferably at bedtime
INSTI plus One NNRTI		
Cabenuva (CAB IM and RPV IM)	Cabenuva 600-mg/900-mg kit contains: • CAB 600-mg/3-mL vial and RPV 900-mg/3-mL vial Cabenuva 400-mg/600-mg kit contains: • CAB 400-mg/2-mL vial and RPV 600-mg/2-mL vial	Optional Lead-in with Oral CAB and RPV • CAB 30 mg and RPV 25 mg PO once daily with food for 4 weeks Monthly IM CAB and RPV • Loading dose: CAB 600 mg/3 mL IM × 1 dose and RPV 900 mg/3 mL IM × 1 dose • Continuation phase: CAB 400 mg/2 mL IM every 4 weeks and RPV 600 mg/2 mL IM every 4 weeks Every 2-Month IM CAB and RPV • Loading dose: CAB 600 mg/3 mL IM and RPV 900 mg/3 mL IM once monthly for 2 doses • Continuation phase: CAB 600 mg/3 mL IM and RPV 900 mg/3 mL IM every 2 months
Juluca (DTG/RPV)	Dolutegravir 50 mg/rilpivirine 25 mg	One tablet PO once daily with food

[a] For dose adjustments in patients with renal or hepatic insufficiency, see Appendix B, Table 12. When no food restriction is listed, the product can be taken with or without food.

Key: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; BIC = bictegravir; CAB = cabotegravir; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; IM = intramuscular; INSTI = integrase strand transfer inhibitor; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PO = orally; RPV = rilpivirine; 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

Updated: May 26, 2023
Reviewed: May 26, 2023

The following table includes dose recommendations for U.S. Food and Drug Administration (FDA)–approved dual nucleoside reverse transcriptase inhibitor fixed-dose combination (FDC) products for adults with HIV. For information regarding the use of these medications in adolescents with HIV, including weight limitations and additional dosage forms, please consult FDA product labeling or the Pediatric Antiretroviral Guidelines. These FDC tablets are not complete regimens and must be administered in combination with other antiretroviral drugs. FDC products that contain zidovudine (ZDV) have been removed from this table. Please refer to the FDA product labels for information regarding ZDV-containing FDCs. Please see the class-specific drug characteristics tables (Appendix B, Tables 3, 4, 5, and 6) for details about the individual drugs contained in these FDC products, including information on elimination and metabolic pathways, serum and intracellular half-lives, and adverse effects. The FDC tablets in this table are listed by trade name.

Trade Name (Abbreviation)	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 PO once daily
Cimduo (TDF/3TC)	Tenofovir disoproxil fumarate 300 mg/lamivudine 300 mg	One tablet PO once daily
Truvada (TDF/FTC)	Tenofovir disoproxil fumarate 300 mg/emtricitabine 200 mg	One tablet PO once daily
Other NRTI-Based, FDC Tablets		
Epzicom (ABC/3TC) Note: Generic product is available.	Abacavir 600 mg/lamivudine 300 mg	One tablet PO once daily

[a] For dose adjustments in patients with renal or hepatic insufficiency, see Appendix B, Table 12. All FDC tablets listed in this table can be taken without regard to food.

Key: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; FDC = fixed-dose combination; FTC = emtricitabine; NRTI = nucleoside reverse transcriptase inhibitor; PO = orally; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Appendix B, Table 3. Characteristics of Nucleoside Reverse Transcriptase Inhibitors

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The following table includes dose recommendations for U.S. Food and Drug Administration (FDA)–approved nucleoside reverse transcriptase inhibitor products for adults with HIV. For information regarding the use of these medications in adolescents with HIV, including weight limitations and additional dosage forms, please consult FDA product labeling or the Pediatric Antiretroviral Guidelines. The older nucleoside reverse transcriptase inhibitors didanosine (ddI) and stavudine (d4T) have been discontinued in the United States. Zidovudine (ZDV) is no longer used commonly in clinical practice. Therefore, these antiretrovirals have been removed from this table. Please refer to the U.S. FDA product label for ZDV for information regarding this drug.

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 Generic • 300-mg tablet • Also available as FDC with 3TC FDC Tablets That Contain ABC[c] • Epzicom (ABC/3TC) STRs That Contain ABC[d] • Triumeq (DTG/ABC/3TC)	Ziagen • ABC 600 mg PO once daily, *or* • ABC 300 mg PO twice daily See Appendix B, Tables 1 and 2 for dosing information for FDC tablets that contain ABC.	Metabolized by alcohol dehydrogenase and glucuronyl transferase 82% of ABC dose is excreted in the urine as metabolites of ABC. Dose adjustment is recommended in patients with hepatic insufficiency (see Appendix B, Table 12).	1.5 hours/12–26 hours	Patients who test positive for HLA-B*5701 are at the highest risk of experiencing HSRs. HLA screening should be done before initiating ABC. For patients with a history of HSRs, rechallenge is not recommended. Symptoms of HSRs may include fever, rash, nausea, vomiting, diarrhea, abdominal pain, malaise, fatigue, or respiratory symptoms (e.g., sore throat, cough, or shortness of breath). Some cohort studies suggest an increased risk of MI with recent or current use of ABC, but this risk is not substantiated in other studies.
Emtricitabine (FTC) *Emtriva*	Emtriva • 200-mg hard gelatin capsule • 10-mg/mL oral solution FDC Tablets That Contain FTC[c] • Descovy (TAF/FTC)	Emtriva *Capsule* • FTC 200 mg PO once daily *Oral Solution* • FTC 240 mg (24 mL) PO once daily	86% of FTC dose is excreted renally. See Appendix B, Table 12 for dosing recommendations in patients with renal insufficiency.	10 hours/ >20 hours	Minimal toxicity Hyperpigmentation/skin discoloration Severe acute exacerbation of hepatitis may occur in patients with HBV/HIV coinfection who discontinue FTC.

Appendix B, Table 3. Characteristics of Nucleoside Reverse Transcriptase Inhibitors

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum/ Intracellular Half-Lives	Adverse Events[b]
	• 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)	See Appendix B, Tables 1 and 2 for dosing information for FDC tablets that contain FTC.			
Lamivudine (3TC) *Epivir* Note: Generic products are available.	Epivir • 150-mg and 300-mg tablets • 10-mg/mL oral solution Generic • 150-mg and 300-mg tablets • Also available as FDC with ABC FDC Tablets That Contain 3TC[c] • Cimduo (TDF/3TC) • Epzicom (ABC/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 PO once daily, *or* • 3TC 150 mg PO twice daily See Appendix B, Tables 1 and 2 for dosing information for FDC tablets that contain 3TC.	70% of 3TC dose is excreted renally. See Appendix B, Table 12 for dose recommendations in patients with renal insufficiency.	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

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum/ Intracellular Half-Lives	Adverse Events[b]
Tenofovir Alafenamide (TAF) *Vemlidy* Note: Vemlidy is available as a 25-mg tablet for the treatment of HBV.	FDC Tablets That Contain TAF[c] • Descovy (TAF/FTC) STRs That Contain TAF[d] • Biktarvy (BIC/TAF/FTC) • Genvoya (EVG/c/TAF/FTC) • Odefsey (RPV/TAF/FTC) • Symtuza (DRV/c/TAF/FTC)	See Appendix B, Tables 1 and 2 for dosing information for FDC tablets that contain TAF.	Metabolized by cathepsin A See Appendix B, Table 12 for dosing recommendations in patients with renal insufficiency.	0.5 hour/ 150–180 hours	Renal insufficiency, Fanconi syndrome, and proximal renal tubulopathy are less likely to occur with TAF than with TDF. Osteomalacia and decreases in BMD are less likely to occur with TAF than with TDF. Severe acute exacerbation of hepatitis may occur in patients with HBV/HIV coinfection who discontinue TAF. Diarrhea, nausea, headache Greater weight increase has been reported with TAF than with TDF.
Tenofovir Disoproxil Fumarate (TDF) *Viread* Note: Generic product is available.	Viread • 300-mg tablet • 40-mg/g oral powder Generic • 300-mg tablet FDC Tablets that Contain TDF[c] • Cimduo (TDF/3TC) • Truvada (TDF/FTC) STRs that Contain TDF[d] • Atripla (EFV/TDF/FTC) • Complera (RPV/TDF/FTC) • Delstrigo (DOR/TDF/3TC)	Viread • TDF 300 mg PO once daily, *or* • 7.5 level scoops of oral powder PO 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.	Renal excretion is the primary route of elimination. See Appendix B, Table 12 for dose recommendations in patients with renal insufficiency.	17 hours/ >60 hours	Renal insufficiency, Fanconi syndrome, proximal renal tubulopathy Osteomalacia, decrease in BMD Asthenia, headache, diarrhea, nausea, vomiting, flatulence Severe acute exacerbation of hepatitis may occur in patients with HBV/HIV coinfection who discontinue TDF.

Appendix B, Table 3. Characteristics of Nucleoside Reverse Transcriptase Inhibitors

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum/ Intracellular Half-Lives	Adverse Events[b]
	• Stribild (EVG/c/TDF/FTC) • Symfi (EFV 600 mg/TDF/3TC) • Symfi Lo (EFV 400 mg/TDF/3TC)	See Appendix B, Tables 1 and 2 for dosing information for FDC tablets that contain TDF.			

[a] For dose adjustments in patients with renal or hepatic insufficiency, see Appendix B, Table 12. When no food restriction is listed, the antiretroviral drug can be taken with or without food.

[b] Also see Table 20.

[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; BMD = bone mineral density; DOR = doravirine; DRV/c = darunavir/cobicistat; DTG = dolutegravir; EFV = efavirenz; EVG/c = elvitegravir/cobicistat; FDC = fixed-dose combination; FTC = emtricitabine; HBV = hepatitis B virus; HLA = human leukocyte antigen; HSR = hypersensitivity reaction; MI = myocardial infarction; PO = orally; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Appendix B, Table 4. Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors

Appendix B, Table 4. Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors

Updated: May 26, 2023
Reviewed: May 26, 2023

The following table includes dose recommendations for U.S. Food and Drug Administration (FDA)–approved non-nucleoside reverse transcriptase inhibitor products for adults with HIV. For information regarding the use of these medications in adolescents with HIV, including weight limitations and additional dosage forms, please consult FDA product labeling or the Pediatric Antiretroviral Guidelines. The older non-nucleoside reverse transcriptase inhibitor delavirdine (DLV) has been discontinued in the United States and is **not** listed in this table.

Generic Name (Abbreviation) *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 • DOR 100 mg PO once daily See Appendix B, Table 1 for dosing information for Delstrigo.	CYP3A4/5 substrate	15 hours	Nausea Dizziness Abnormal dreams
Efavirenz (EFV) Note: The branded product Sustiva has been discontinued.	Efavirenz (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)	Efavirenz (generic) • EFV 600 mg PO 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 QT interval prolongation Use of EFV may lead to false-positive results with some cannabinoid and benzodiazepine screening assays.
Etravirine (ETR) *Intelence*	Intelence • 100-mg and 200-mg tablets	Intelence • ETR 200 mg PO 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.

Appendix B, Table 4. Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/Metabolic Pathway	Serum Half-Life	Adverse Events[b]
					Nausea
Nevirapine (NVP) *Viramune* *Viramune XR* Note: Generic products are available.	Viramune • 200-mg tablet • 50-mg/5-mL oral suspension Viramune XR • 400-mg tablet Generic • 200-mg tablet • 400-mg extended-release tablet • 50-mg/5-mL oral suspension	Viramune • NVP 200 mg PO once daily for 14 days (lead-in period); thereafter, NVP 200 mg PO twice daily, *or* • NVP 400 mg (Viramune XR tablet) PO once daily Take without regard to food. Repeat lead-in period if therapy is discontinued for >7 days. In patients who develop mild-to-moderate rash without constitutional symptoms, continue lead-in dose until rash resolves, but do not extend lead-in period beyond 28 days.	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 12).	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 Coformulated STRs that Contain RPV[c] • Complera (RPV/TDF/FTC) • Juluca (DTG/RPV) • Odefsey (RPV/TAF/FTC) Copackaged Intramuscular Regimen • Cabenuva (CAB plus RPV)	Edurant • RPV 25 mg PO once daily Take with food. See Appendix B, Table 1 for dosing information for coformulated and copackaged regimens that contain RPV.	CYP3A4 substrate	PO: 50 hours IM: 13–28 weeks	Rash[d] Depression, insomnia, headache Hepatotoxicity QT interval prolongation IM Formulation Only • Injection-site reactions (pain, induration, swelling, nodules) • Rare post-injection reaction (dyspnea, agitation, abdominal cramps, flushing) occurring within a few minutes after RPV IM injection; possibly associated with inadvertent IV administration.

[a] For dose adjustments in patients with renal or hepatic insufficiency, see Appendix B, Table 12. When no food restriction is listed, the antiretroviral drug can be taken with or without food.

Appendix B, Table 4. Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors

[b] Also see Table 20.

[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 who are receiving EFV may experience any of these symptoms. Symptoms usually subside spontaneously after 2–4 weeks, but discontinuation of EFV may be necessary in a small percentage of patients. Late-onset neurotoxicities, including ataxia and encephalopathy, have been reported.

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

Appendix B, Table 5. Characteristics of Protease Inhibitors

Updated: May 26, 2023
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The following table includes dose recommendations for U.S. Food and Drug Administration (FDA)–approved protease inhibitor products for adults with HIV. For information regarding the use of these medications in adolescents with HIV, including weight limitations and additional dosage forms, please consult FDA product labeling or the Pediatric Antiretroviral Guidelines. The older protease inhibitors indinavir (IDV) and saquinavir (SQV) have been discontinued in the United States; fosamprenavir (FPV), nelfinavir (NFV), and tipranavir (TPV) are no longer used commonly in clinical practice. These agents have been removed from this table. Please refer to the July 10, 2019, version of the guidelines (found in the Adult and Adolescent Antiretroviral Archived Guidelines section of Clinicalinfo) or to the U.S. Food and DrugFDA product labels for information regarding these drugs.

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum Half-Life	Adverse Events[b]
Atazanavir (ATV) *Reyataz* (ATV/c) *Evotaz* Note: Generic products of ATV are available.	Reyataz • 200-mg and 300-mg capsules • 50-mg oral powder/packet Generic • 200-mg and 300-mg capsules Evotaz • ATV 300-mg/COBI 150-mg tablet	Reyataz *In ARV-Naive Patients* • (ATV 300 mg plus RTV 100 mg) PO once daily; *or* • ATV 400 mg PO once daily • Take with food. *With TDF or in ARV-Experienced Patients* • (ATV 300 mg plus RTV 100 mg) PO once daily • Unboosted ATV is not recommended. • Take with food. *With EFV in ARV-Naive Patients* • (ATV 400 mg plus RTV 100 mg) PO once daily • Take with food. Evotaz • One tablet PO once daily • Take with food.	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 12).	7 hours	Indirect hyperbilirubinemia 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. 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.

Appendix B, Table 5. Characteristics of Protease Inhibitors

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum Half-Life	Adverse Events[b]
		• The use of ATV/c **is not recommended** for patients who are taking TDF and who have baseline CrCl <70 mL/min (see Appendix B, Table 12 for the equation for calculating CrCl). For dosing recommendations for patients who also are receiving H2 antagonists and PPIs, refer to Table 24a.			
Darunavir (DRV) *Prezista* (DRV/c) *Prezcobix*	Prezista • 600-mg 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) PO once daily • Take with food. *In ARV-Experienced Patients with One or More DRV Resistance Mutations* • (DRV 600 mg plus RTV 100 mg) PO twice daily • Take with food. Unboosted DRV **is not recommended**. Prezcobix • One tablet PO 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 12 for the equation for calculating CrCl).	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	Hepatotoxicity Diarrhea, nausea Headache Hyperlipidemia Serum transaminase elevation Hyperglycemia Fat maldistribution An increase in serum creatinine may occur when DRV is administered with COBI. Skin rash: DRV has a sulfonamide moiety; however, incidence and severity of rash are similar in those with or without a sulfonamide allergy—Stevens-Johnson syndrome, toxic epidermal necrolysis, acute generalized exanthematous pustulosis, and erythema multiforme have been reported.

Appendix B, Table 5. Characteristics of Protease Inhibitors

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum Half-Life	Adverse Events[b]
		See Appendix B, Table 1 for dosing information for Symtuza.			
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 PO twice daily, *or* • LPV/r 800 mg/200 mg PO once daily. However, once-daily dosing is not recommended for patients with three or more LPV-associated mutations, pregnant persons, or patients receiving EFV, NVP, carbamazepine, phenytoin, or phenobarbital. *With EFV or NVP in PI-Naive or PI-Experienced Patients* • LPV/r 500-mg/125-mg tablets PO 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 food. *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.

Appendix B, Table 5. Characteristics of Protease Inhibitors

Generic Name (Abbreviation) *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 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 PO per day in one or two divided doses (refer to other PIs for specific dosing recommendations). Food Restrictions • Take with food.	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

[a] For dose adjustments in patients with hepatic insufficiency, see Appendix B, Table 12.

[b] Also see Table 20.

Key: ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; AV = atrioventricular; COBI = cobicistat; CrCl = creatinine clearance; CYP = cytochrome P; DRV = darunavir; DRV/c = darunavir/cobicistat; EFV = efavirenz; FDC = fixed-dose combination; FTC = emtricitabine; GI = gastrointestinal; H2 = histamine H2 receptor; LPV = lopinavir; LPV/r = lopinavir/ritonavir; NVP = nevirapine; PI = protease inhibitor; PK = pharmacokinetic; PO = orally; PPI = proton pump inhibitor; RTV = ritonavir; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; UGT1 = uridine diphosphate glucuronyl transferase 1 family

Appendix B, Table 6. Characteristics of Integrase Strand Transfer Inhibitors

Updated: May 26, 2023
Reviewed: May 26, 2023

The following table includes dose recommendations for U.S. Food and Drug Administration (FDA)–approved integrase strand transfer inhibitor products for adults with HIV. Not all products are FDA-approved for adolescents with HIV. For information regarding the use of these medications in adolescents with HIV, including weight limitations and additional dosage forms, please consult FDA product labeling or the Pediatric Antiretroviral Guidelines.

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathways	Serum Half-Life	Adverse Events[b]
Bictegravir (BIC)	BIC is available only as a component of the STR Biktarvy (BIC/TAF/FTC).[c]	Biktarvy • One tablet PO once daily	CYP3A4 substrate UGT1A1-mediated glucuronidation	~17 hours	Diarrhea Nausea Headache Weight gain
Cabotegravir (CAB)	Available as part of the copackaged IM long-acting regimen Cabenuva (CAB IM and RPV IM) • 400-mg/2-mL vial • 600-mg/3-mL vial Also available as an individual product for IM long-acting pre-exposure prophylaxis Apretude (CAB IM) • 600-mg/3-mL vial Also available in oral tablet formulation Vocabria (CAB PO) • 30-mg tablet • Must be obtained from manufacturer for oral lead-in and oral bridging during administration of Cabenuva (CAB IM/RPV IM)	See Appendix B, Table 1 for dosing information for coformulated and copackaged regimens that contain CAB.	UGT1A1 and UGT1A9-mediated glucuronidation	Oral: 41 hours IM: 6–12 weeks	Headache Nausea Abnormal dreams Anxiety Insomnia Depressive disorders Hepatotoxicity IM formulation only: Injection-site reactions (e.g., pain, induration, swelling, nodules)

Appendix B, Table 6. Characteristics of Integrase Strand Transfer Inhibitors

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathways	Serum Half-Life	Adverse Events[b]
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 PO once daily In ARV-Naive or ARV-Experienced, INSTI-Naive Patients when Coadministered with EFV, FPV/r, TPV/r, or Rifampin • DTG 50 PO mg twice daily In INSTI-Experienced Patients with Certain INSTI Mutations (See Product Label) or with Clinically Suspected INSTI Resistance • DTG 50 mg PO 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 preexisting psychiatric conditions) Weight gain Hepatotoxicity Potential for increased risk of NTDs in infants born to individuals who received DTG around the time of conception is lower than previously reported. Refer to Appendix B, Table 6 for more information. HSRs, including rash, constitutional symptoms, and organ dysfunction (including liver injury), have been reported.
Elvitegravir (EVG)	EVG is only available as a component of an STR tablet that also contains COBI, FTC, and either TDF or TAF. STRs that Contain EVG[c] • Genvoya (EVG/c/TAF/FTC) • Stribild (EVG/c/TDF/FTC)	Genvoya • One tablet PO once daily with food • See Appendix B, Table 12 for recommendations on dosing in persons with renal insufficiency. Stribild • One tablet PO once daily with food • Not recommended for patients with baseline CrCl <70 mL/min (see Appendix B, Table 12 for the CrCl calculation equation).	EVG • CYP3A and UGT1A1/3 substrate COBI • CYP3A inhibitor and substrate • CYP2D6 inhibitor	EVG/c: ~13 hours	Nausea Diarrhea Depression and suicidal ideation (rare; usually occurs in patients with preexisting psychiatric conditions)

Appendix B, Table 6. Characteristics of Integrase Strand Transfer Inhibitors

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 • 100-mg single-use packet for oral suspension Isentress HD • 600-mg tablet	Isentress *In ARV-Naive Patients or ARV-Experienced Patients* • 400 mg PO twice daily *With Rifampin* • 800 mg PO twice daily Isentress HD *In ARV-Naive or ARV-Experienced Patients with Virologic Suppression on a Regimen Containing RAL 400 mg Twice Daily* • 1,200 mg (two 600-mg tablets) PO once daily *With Rifampin* • Not recommended	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 Weight gain Insomnia Depression and suicidal ideation (rare; usually occurs in patients with preexisting psychiatric conditions)

[a] For dose adjustments in patients with hepatic insufficiency, see Appendix B, Table 12. When no food restriction is listed, the antiretroviral drug can be taken with or without food.

[b] Also see Table 20.

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

Key: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; BIC = bictegravir; CAB = cabotegravir; COBI = cobicistat; CPK = creatine phosphokinase; CrCl = creatinine clearance; CYP = cytochrome P; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; HSR = hypersensitivity reaction; IM = intramuscular; INSTI = integrase strand transfer inhibitor; NTD = neural tube defect; PO = orally; RAL = raltegravir; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV/r = tipranavir/ritonavir; UGT1 = uridine diphosphate glucuronyl transferase 1 family

Appendix B, Table 7. Characteristics of the Fusion Inhibitor

Updated: May 26, 2023
Reviewed: May 26, 2023

The following table includes dose recommendations for the U.S. Food and Drug Administration (FDA)–approved fusion inhibitor. For additional information regarding the use of this medication in adolescents with HIV, please consult FDA product labeling or the Pediatric Antiretroviral Guidelines.

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 20.

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

Appendix B, Table 8. Characteristics of the CCR5 Antagonist

Updated: May 26, 2023
Reviewed: May 26, 2023

The following table includes dose recommendations for the U.S. Food and Drug Administration (FDA)–approved CCR5 antagonist. For additional information regarding the use of this medication in adolescents with HIV, please consult FDA product labeling or the Pediatric Antiretroviral Guidelines.

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations[a]	Serum Half-Life	Elimination/ Metabolic Pathway	Adverse Events[b]
Maraviroc (MVC) *Selzentry*	Selzentry • 150-mg and 300-mg tablets • 20-mg/1-mL oral solution	Selzentry • MVC 150 mg PO twice daily when given with drugs that are strong CYP3A inhibitors (with or without CYP3A inducers), including PIs (except TPV/r) • MVC 300 mg PO twice daily when given with NRTIs, T-20, TPV/r, NVP, RAL, and other drugs that are not strong CYP3A inhibitors or inducers • MVC 600 mg PO twice daily when given with drugs that are CYP3A inducers, including EFV, ETR, etc. (without a CYP3A inhibitor) Take MVC without regard to food.	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 12.

[b] Also see Table 20.

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

Appendix B, Table 9. Characteristics of the CD4 Post-Attachment Inhibitor

Updated: May 26, 2023
Reviewed: May 26, 2023

The following table includes dose recommendations for the U.S. Food and Drug Administration (FDA)–approved CD4 post-attachment inhibitor. Ibalizumab is not Food and Drug Administration-approved for use in adolescents with HIV.

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 or IV push over 30 seconds 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 Hypersensitivity, including anaphylaxis and infusion-related reactions, have been reported.

Key: IBA = ibalizumab; IV = intravenous

Appendix B, Table 10. Characteristics of the gp120 Attachment Inhibitor

Updated: May 26, 2023
Reviewed: May 26, 2023

The following table includes dose recommendations for the U.S. Food and Drug Administration (FDA)–approved gp120 attachment inhibitor. Fostemsavir is not Food and Drug Administration-approved for use in adolescents with HIV.

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Serum Half-Life	Elimination/ Metabolic Pathway	Adverse Events
Fostemsavir (FTR) *Rukobia*	• 600-mg extended-release tablets	• FTR 600 mg PO twice daily	11 hours	Hydrolysis (esterases), CYP3A4	Nausea Transaminase elevation; transient bilirubin elevation Sleep disturbance, dizziness QTc prolongation was seen at 4 times the recommended dose. Use with caution in patients with preexisting heart disease, QTc prolongation, or concomitant use of medications that may prolong QTc interval.

Key: CYP = cytochrome P; FTR = fostemsavir; PO = orally; QTc = corrected QT interval

Appendix B, Table 11. Characteristics of the Capsid Inhibitor

Updated: May 26, 2023
Reviewed: May 26, 2023

The following table includes dose recommendations for the U.S. Food and Drug Administration (FDA)–approved capsid inhibitor. Lenacapavir is not Food and Drug Administration-approved for use in adolescents with HIV.

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Serum Half-Life	Elimination/ Metabolic Pathway	Adverse Events
Lenacapavir (LEN) *Sunlenca*	• 300-mg tablet • Single-dose 463.5-mg/1.5-mL vial for injection	Initiation Option 1 • Day 1: 927 mg SQ x 1 dose + 600 mg PO x 1 dose • Day 2: 600 mg PO x 1 dose Initiation Option 2 • Day 1: 600 mg PO x 1 dose • Day 2: 600 mg PO x 1 dose • Day 8: 300 mg PO x 1 dose • Day 15: 927 mg SQ x 1 dose Maintenance Dosing • 927 mg by SQ injection every 6 months from the date of the last injection (+/-2 weeks)	PO: 10–12 days SQ: 8–12 weeks	Substrate of P-glycoprotein, CYP3A (minor), UGT1A1 (minor) CYP3A4 inhibitor (moderate)	Nausea, diarrhea, headache Injection site reactions

Key: CYP = cytochrome P; LEN = lenacapavir; PO = orally; SQ = subcutaneous

Appendix B, Table 12. Antiretroviral Dosing Recommendations in Adults with Renal or Hepatic Insufficiency

Updated: May 26, 2023
Reviewed: May 26, 2023

Not all products are Food and Drug Administration (FDA)-approved for adolescents with HIV. For information regarding the use of these medications in adolescents with HIV, including weight limitations and additional dosage forms, please consult FDA product labeling or the Pediatric Antiretroviral Guidelines.

The older antiretroviral drugs fosamprenavir (FPV), nelfinavir (NFV), tipranavir (TPV), and zidovudine (ZDV) have been removed from this table. Please refer to the FDA product labels for these drugs for recommendations on dosing in adults and adolescents with renal or hepatic insufficiency.

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

Generic Name (Abbreviation) *Trade Name*	Usual Dose[a]	Dosing in Adults with Renal Insufficiency	Dosing in Adults with Hepatic Impairment
Some FDC products are not recommended in persons with different degrees of renal insufficiency. The recommendations for individual FDCs based on CrCl level are outlined below. • *CrCl <70 mL/min:* Initiation of Stribild is not recommended. • *CrCl <50 mL/min:* FDCs not recommended: Atripla, Cimduo, Complera, Delstrigo, Truvada, Symfi, Symfi-Lo • *CrCl <30 mL/min:* FDCs not recommended: Dovato, Epzicom, Triumeq • *CrCl <30 mL/min and not on HD:* FDCs not recommended: Biktarvy, Descovy, Genvoya, Odefsey, and Symtuza. The component drugs in some of the FDC products listed above may be prescribed as individual formulations with dose adjustment based on CrCl level as indicated below in this table.			
NRTIs			
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

Appendix B, Table 12. Antiretroviral Dosing Recommendations in Adults with Renal or Hepatic Insufficiency

<table>
<tr><th>Generic Name
(Abbreviation)
Trade Name</th><th>Usual Dose[a]</th><th>Dosing in Adults with Renal Insufficiency</th><th>Dosing in Adults with Hepatic Impairment</th></tr>
<tr><td>Abacavir/Lamivudine
(ABC/3TC)
Epzicom</td><td>One tablet PO once daily</td><td>Not recommended if CrCl <30 mL/min. Instead, use the individual component drugs and adjust 3TC dose according to CrCl.</td><td>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</td></tr>
<tr><td>Emtricitabine
(FTC)
Emtriva</td><td>FTC 200-mg oral capsule once daily

or

FTC 240-mg (24-mL) oral solution once daily</td><td>Dose by Formulation
<table><tr><th>CrCl (mL/min)</th><th>Capsule</th><th>Solution</th></tr><tr><td>30–49</td><td>200 mg every 48 hours</td><td>120 mg every 24 hours</td></tr><tr><td>15–29</td><td>200 mg every 72 hours</td><td>80 mg every 24 hours</td></tr><tr><td><15</td><td>200 mg every 96 hours</td><td>60 mg every 24 hours</td></tr><tr><td>On HD[b]</td><td>200 mg every 24 hours</td><td>240 mg every 24 hours</td></tr></table></td><td>No dose recommendation.</td></tr>
<tr><td>Lamivudine[c]
(3TC)
Epivir</td><td>3TC 300 mg PO once daily

or

3TC 150 mg PO twice daily</td><td><table><tr><th>CrCl (mL/min)</th><th>Dose</th></tr><tr><td>15–29</td><td>1 × 150 mg, then 100 mg every 24 hours</td></tr><tr><td>5–14</td><td>1 × 150 mg, then 50 mg every 24 hours</td></tr><tr><td><5 or on HD</td><td>1 × 50 mg, then 25 mg every 24 hours</td></tr></table></td><td>No dose adjustment necessary.</td></tr>
</table>

Appendix B, Table 12. Antiretroviral Dosing Recommendations in Adults with Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	Usual Dose[a]	Dosing in Adults with Renal Insufficiency		Dosing in Adults with Hepatic Impairment
Tenofovir Alafenamide (TAF) *Vemlidy*	Vemlidy is available as a 25-mg tablet for the treatment of HBV.	CrCl (mL/min)	Dose	*Child-Pugh Class B or C:* Not recommended
		<15 and not on HD	Not recommended	
		On HD	One tablet PO once daily	
Tenofovir Alafenamide/Emtricitabine (TAF/FTC) *Descovy*	TAF for HIV treatment is only available as a component of FDC tablets (i.e., in Descovy, Genvoya, Odefsey, Biktarvy, and Symtuza). TAF 10 mg PO daily with EVG/c (Genvoya) or DRV/c (Symtuza) TAF 25 mg PO daily in other FDC tablets	CrCl (mL/min)	Dose	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C*: No dose recommendation
		<30 and not on HD	Not recommended	
		<30 and on HD	One tablet once daily	
Tenofovir Disoproxil Fumarate (TDF) *Viread*	TDF 300 mg PO once daily	CrCl (mL/min)	Dose	No dose adjustment necessary.
		30–49	300 mg every 48 hours	
		10–29	300 mg twice weekly (every 72–96 hours)	
		<10 and not on HD	No recommendation	
		On HD	300 mg every 7 days	
Tenofovir Disoproxil Fumarate/Emtricitabine (TDF/FTC) *Truvada*	One tablet PO once daily	CrCl (mL/min)	Dose	No dose recommendation.
		30–49	One tablet every 48 hours	
		<30 or on HD	Not recommended	
Tenofovir Disoproxil Fumarate/Lamivudine (TDF/3TC) *Cimduo*	One tablet PO once daily	CrCl (mL/min)	Dose	No dose recommendation.
		<50 or on HD	Not recommended	
NNRTIs				

Appendix B, Table 12. Antiretroviral Dosing Recommendations in Adults with Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	Usual Dose[a]	Dosing in Adults with Renal Insufficiency	Dosing in Adults with Hepatic Impairment
Doravirine (DOR) *Pifeltro*	DOR 100 mg PO once daily	No dose adjustment required in mild, moderate, or severe renal impairment. Has not been studied in individuals with ESRD or on HD.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* Not studied
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 PO once daily on an empty stomach, preferably at bedtime	**Not recommended** if CrCl <50 mL/min. Instead, use the individual component ARVs 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 PO 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 component ARVs and adjust TDF and 3TC doses according to CrCl level.	**Not recommended** for patients with moderate or severe hepatic impairment. Use with caution in patients with mild hepatic impairment.
Efavirenz 400 mg/Tenofovir Disoproxil Fumarate/Lamivudine (EFV/TDF/3TC) *Symfi Lo*	One tablet PO 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 component ARVs and adjust TDF and 3TC doses according to CrCl level.	**Not recommended** for patients with moderate or severe hepatic impairment. Use with 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

Appendix B, Table 12. Antiretroviral Dosing Recommendations in Adults with Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	Usual Dose[a]	Dosing in Adults with Renal Insufficiency	Dosing in Adults with Hepatic Impairment
Nevirapine (NVP) *Viramune* *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 PO) *Edurant*	RPV 25 mg PO once daily	No dose adjustment necessary.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No dose recommendation
Rilpivirine IM plus Cabotegravir IM (RPV IM and CAB IM) *Cabenuva*	Monthly Dosing • Loading dose: RPV 900 mg/3 mL IM × 1 dose and CAB 600 mg/3 mL IM × 1 dose • Continuation phase: RPV 600 mg/2 mL IM every 4 weeks and CAB 400 mg/2 mL IM every 4 weeks Every 2-Month Dosing • Loading dose: RPV 900 mg/3 mL IM and CAB 600 mg/3 mL IM monthly for 2 doses • Continuation phase: RPV 900 mg/3 mL IM and CAB 600 mg/3 mL IM every 2 months	No dose adjustment necessary for mild or moderate renal impairment. For patients with severe renal impairment or on HD, increase monitoring for adverse events.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No recommendation
Rilpivirine/Tenofovir Alafenamide/Emtricitabine (RPV/TAF/FTC) *Odefsey*	One tablet PO once daily	In Patients on Chronic HD • One tablet once daily. On HD days, administer after dialysis. Not recommended in patients with CrCl <30 mL/min who are not receiving chronic HD.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No dose recommendation

Appendix B, Table 12. Antiretroviral Dosing Recommendations in Adults with Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	Usual Dose[a]	Dosing in Adults with Renal Insufficiency	Dosing in Adults with Hepatic Impairment
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 component ARVs and adjust TDF and FTC doses according to CrCl level.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No dose recommendation
Rilpivirine/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 are not recommended	*Child-Pugh Class A:* No dose adjustment *Child-Pugh Class B:* ATV 300 mg once daily (unboosted) for ARV-naive patients only *Child-Pugh Class C:* Not recommended RTV boosting is not recommended in patients with hepatic impairment.
Atazanavir/Cobicistat (ATV/c) *Evotaz*	One tablet PO once daily	If Used with TDF • Not recommended if CrCl <70 mL/min	Not recommended in patients with hepatic impairment.
Darunavir (DRV) *Prezista*	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

Appendix B, Table 12. Antiretroviral Dosing Recommendations in Adults with Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	Usual Dose[a]	Dosing in Adults with Renal Insufficiency	Dosing in Adults with Hepatic Impairment
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
Darunavir/Cobicistat/Tenofovir Alafenamide/Emtricitabine (DRV/c/TAF/FTC) *Symtuza*	One tablet PO once daily	In Patients on Chronic HD • One tablet once daily. On HD days, administer after dialysis. Not recommended in patients with CrCl <30 mL/min who are not receiving chronic HD.	Not recommended for patients with severe hepatic impairment.
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.
Ritonavir (RTV) *Norvir*	As a PI-Boosting Agent • RTV 100–400 mg PO per day	No dose adjustment necessary.	Refer to recommendations for the primary (i.e., boosted) PI.
INSTIs			
Bictegravir/Tenofovir Alafenamide/Emtricitabine (BIC/TAF/FTC) *Biktarvy*	One tablet PO once daily	In Patients on Chronic HD • One tablet once daily. On HD days, administer after dialysis. • Patients receiving chronic HD should be virologically suppressed before Biktarvy is initiated. Not recommended in patients with CrCl <30 mL/min who are not receiving chronic HD.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* Not recommended

Appendix B, Table 12. Antiretroviral Dosing Recommendations in Adults with Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	Usual Dose[a]	Dosing in Adults with Renal Insufficiency	Dosing in Adults with Hepatic Impairment
Cabotegravir (CAB PO) *Vocabria*	Treatment (As Optional Oral Lead-In or As Oral Bridging) • CAB 30 mg PO once daily, given with RPV 25 mg PO, with food before switching to CAB IM and RPV IM Pre-exposure Prophylaxis (Optional Oral Lead-In) • CAB 30 mg PO once daily before switching to CAB IM	No dose adjustment necessary.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No recommendation
Cabotegravir (CAB IM) *Apretude*	Pre-exposure Prophylaxis • Loading dose: CAB 600 mg/3 mL IM monthly for 2 doses • Continuation phase: CAB 600 mg/3 mL IM every 2 months	No dose adjustment necessary.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No recommendation
Cabotegravir IM plus Rilpivirine IM (CAB IM plus RPV IM) *Cabenuva*	Monthly Dosing • Loading dose: CAB 600 mg/3 mL IM × 1 dose and RPV 900 mg/3 mL IM × 1 dose • Continuation phase: CAB 400 mg/2 mL IM every 4 weeks and RPV 600 mg/2 mL IM every 4 weeks Every 2-Month Dosing • Loading dose: CAB 600 mg/3 mL IM and RPV 900 mg/3 mL IM monthly for 2 doses • Continuation phase: CAB 600 mg/3 mL IM and RPV 900 mg/3 mL IM every 2 months	No dose adjustment necessary for mild or moderate renal impairment. For patients with severe renal impairment or on HD, increase monitoring for adverse events.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No recommendation

Appendix B, Table 12. Antiretroviral Dosing Recommendations in Adults with Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	Usual Dose[a]	Dosing in Adults with Renal Insufficiency	Dosing in Adults with Hepatic Impairment
Dolutegravir (DTG) *Tivicay*	DTG 50 mg PO once daily *or* DTG 50 mg PO 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 PO once daily	Not recommended if CrCl <30 mL/min. Instead, use the individual component 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/Lamivudine (DTG/3TC) *Dovato*	One tablet PO once daily	Not recommended if CrCl <30 mL/min. Instead, use the individual component drugs and adjust 3TC dose according to CrCl.	*Child-Pugh Class C:* Not recommended
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 PO once daily	In Patients on Chronic HD • One tablet once daily. On HD days, administer after dialysis. Not recommended in patients with CrCl <30 mL/min who are not receiving chronic HD.	*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 PO 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

Appendix B, Table 12. Antiretroviral Dosing Recommendations in Adults with Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	Usual Dose[a]	Dosing in Adults with Renal Insufficiency	Dosing in Adults with Hepatic Impairment
Raltegravir (RAL) *Isentress* *Isentress HD*	RAL 400 mg PO twice daily (using Isentress formulation) *or* RAL 1,200 mg PO 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
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; if postural hypotension occurs, reduce to MVC 150 mg twice daily *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: IBA 2,000 mg IV Maintenance dose: IBA 800 mg IV every 2 weeks	No dose adjustment recommended.	No recommendation.
gp-120 Attachment Inhibitor			

Appendix B, Table 12. Antiretroviral Dosing Recommendations in Adults with Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	Usual Dose[a]	Dosing in Adults with Renal Insufficiency	Dosing in Adults with Hepatic Impairment
Fostemsavir (FTR) *Rukobia*	FTR 600 mg PO twice daily	No dose adjustment recommended.	No dose adjustment recommended.
Capsid Inhibitor			
Lenacapavir (LEN) *Sunlenca*	Initiation Option 1 • Day 1: 927 mg SQ x 1 dose plus 600 mg PO x 1 dose • Day 2: 600 mg PO x 1 dose Initiation Option 2 • Day 1: 600 mg PO x 1 dose • Day 2: 600 mg PO x 1 dose • Day 8: 300 mg PO x 1 dose • Day 15: 927 mg SQ x 1 dose Maintenance Dosing • 927 mg by SQ injection every 6 months from the date of the last injection (+/-2 weeks)	No dose adjustment recommended.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No recommendation

[a] Refer to Appendix B, Tables 1–10 for additional dosing information.

[b] The prescribing information for emtricitabine (Emtriva) recommends a dose of 200 mg every 96 hours for patients with CrCl <15 mL/min or on hemodialysis. However, the prescribing information for several FDC products that contain emtricitabine (including Descovy, Biktarvy, Genvoya, and Odefsey) recommends that the standard dose (emtricitabine 200 mg) can be given once daily in these patients (i.e., on the days of hemodialysis, administer standard dose after completion of dialysis). The recommendation in this table incorporates the dosing guidance from the FDC products.

[c] The prescribing information for lamivudine (Epivir) recommends dosage adjustment from 300 mg once daily to 150 mg once daily for patients with CrCl 30–49 mL/min. However, the prescribing information for several FDC products that contain lamivudine (including Epzicom, Dovato, and Triumeq) recommends no dose adjustment for CrCl 30–49 mL/min. The recommendation in this table incorporates the dosing guidance from the FDC products.

Key: 3TC = lamivudine; ABC = abacavir; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; CAB = cabotegravir; COBI = cobicistat; CrCl = creatinine clearance; CYP = cytochrome P; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DTG = dolutegravir; EFV = efavirenz; ESRD = end stage renal disease; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FDC = fixed-dose combination; FTC = emtricitabine; FTR = Fostemsavir; HBV = hepatitis B virus; HD = hemodialysis; IBA = ibalizumab; IM = intramuscular; INSTI = integrase strand transfer inhibitor; IV = intravenous; LEN = lenacapavir; LPV = lopinavir; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PO = orally; RAL = raltegravir;

Appendix B, Table 12. Antiretroviral Dosing Recommendations in Adults with Renal or Hepatic Insufficiency

RPV = rilpivirine; RTV = ritonavir; SQ = subcutaneous; T-20 = enfuvirtide; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; XR = extended release

Appendix B, Table 12. Antiretroviral Dosing Recommendations in Adults with Renal or Hepatic Insufficiency

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

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 is used for patients who have Gilbert's syndrome or who are taking 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.