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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 On some occasions, particularly when new information may affect patient safety, unpublished data presented at major conferences or prepared by the FDA and/or manufacturers as warnings to the public may be used as evidence to revise the guidelines.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

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 Viral Load	√	√	√[e]	√[f]	√[f]		√	√	Repeat testing is optional.
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	√	

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]
HLA-B*5701 Testing		√ If considering ABC							
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

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]
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		√	
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	

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]
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 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

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

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 resistance testing results (AIII). See Early (Acute and Recent) HIV Infection for discussion on ART selection.	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 genotypic resistance testing may be considered when therapy is initiated (CIII). A genotypic assay is preferred (AIII).	Repeat testing when ART is initiated may be considered because the person may have acquired a drug-resistant virus (i.e., superinfection).
Before ART Initiation in People 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 resistance testing results (AIII).	Transmitted HIV with baseline resistance to at least one drug has been reported, and suboptimal virologic responses may be seen in people with baseline resistance mutations to ARVs in the prescribed regimen. Some drug-resistance mutations can remain detectable for years in untreated people with chronic HIV.
If transmitted or acquired INSTI resistance (including among people who had received INSTI for post-exposure prophylaxis) 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-life of CAB-LA, 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). See What to Start for discussion on ART selection.	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 people 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 CAB-LA for PrEP or an INSTI-based regimen for post-exposure prophylaxis.
For pregnant people or people who will initiate ART 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 genotypic 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 person may have acquired a drug-resistant virus (i.e., a superinfection). Genotypic testing is preferred to phenotypic testing because of lower cost, faster turnaround time, and greater sensitivity for detecting mixtures of wild-type and resistant virus.
In People With Virologic Failure Drug-resistance testing is recommended in people on ART with HIV RNA >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 people 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 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.

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

Clinical Setting and Recommendation	Rationale
Resistance testing should be done while the person 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 people with HIV must be interpreted with caution when designing subsequent ARV regimens, as mutations may decay with time.
For people who previously received LA CAB/RPV and present with virologic failure, resistance testing (including INSTI genotypic testing) should be performed regardless of the time since the last dose of LA CAB/RPV (AIII).	Because of the long half-lives of LA CAB and RPV, resistance mutations to INSTI and NNRTI may emerge even months after the last doses of these drugs.
Reverse transcriptase and protease genotypic resistance testing should be performed on people with virologic failure. Integrase resistance testing should be performed on individuals who have virologic failure and have a history of prior use of an INSTI (for prevention or treatment) or are currently receiving an INSTI-based regimen (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. INSTI-resistance tests may need to be ordered separately. (Clinicians should check with the testing laboratory.)
All prior and current drug-resistance testing results should be reviewed and considered when designing a new ARV regimen for a person 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.
Adding phenotypic testing to genotypic testing is generally preferred in people with known or suspected complex drug-resistance patterns (BIII).	Phenotypic testing can provide additional useful information in people with complex drug-resistance mutation patterns.
If use of a CCR5 antagonist is being considered, a co-receptor tropism assay should be performed (AI).	See Co-Receptor Tropism Assays section.
In People With Suboptimal Suppression of Viral Load Drug-resistance testing is recommended in people 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 initial 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 HIV in the pregnant person and to prevent perinatal transmission of HIV. Genotypic resistance testing will assist the clinician in selecting the optimal ARV regimen. However, treatment should not be delayed while awaiting resistance testing results. The initial regimen can be modified once resistance test results are available, if needed.
In People 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 if HIV RNA is below the limit of detection or with low-level viremia, where a HIV RNA genotypic assay is unlikely to be successful (CIII).	HIV-1 proviral DNA resistance assays 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 = long-acting cabotegravir; CCR5 = cysteine-cysteine chemokine receptor 5; INSTI = integrase strand transfer inhibitor; LA = long-acting; LA CAB/RPV = long-acting cabotegravir/rilpivirine; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PrEP = pre-exposure prophylaxis; RPV = rilpivirine

Table 6a. Recommended Initial Regimens for Most People With HIV

Selection of antiretroviral therapy (ART) should be based on the regimen's virologic efficacy, potential adverse effects, pill burden, dosing frequency, drug–drug interaction potential, cost, access, resistance test results, and the comorbid condition of the person with HIV. A pregnancy test should be performed in people 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. Additional initial ARV regimen options for certain clinical scenarios are listed in Table 6b below.

Table 6a. 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 using CAB-LA as PrEP, one of the following regimens is recommended[a]: • BIC/TAF/FTC (AI) • DTG plus (TAF or TDF)[b] plus (FTC or 3TC) (AI) • 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 who have a history of CAB-LA use as PrEP, INSTI genotype resistance testing should be performed before starting ART. If ART is to be started before results of genotypic testing results, the following regimen is recommended: • DRV/c[c] or DRV/r with (TAF or TDF)[b] plus (FTC or 3TC)—pending the results of the genotype test (AIII)
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] Because of the current low rates of transmitted INSTI resistance in the United States, even when there is suspicion that HIV was acquired from a partner with virologic failure while on an INSTI, an INSTI-based regimen can be started pending the results of the INSTI genotype.

[b] TAF and TDF are two forms of TFV approved by the U.S. Food and Drug Administration. TAF has fewer bone and kidney toxicities than TDF, while TDF is associated with lower lipid levels. Safety, cost, and access are among the factors to consider when choosing between these drugs.

[c] COBI should be avoided in pregnancy because lower concentrations of COBI and DRV have been reported during the second and third trimesters. For further information, refer to the Perinatal Guidelines.

Note: The following are available as coformulated drugs: BIC/TAF/FTC, DRV/c/TAF/FTC, DTG/3TC, TAF/FTC, TDF/3TC, and TDF/FTC.

Key: 3TC = lamivudine; ART = antiretroviral therapy; BIC = bictegravir; CAB-LA = long-acting cabotegravir; COBI = cobicistat; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; FTC = emtricitabine; HBV = hepatitis B virus; INSTI = integrase strand transfer inhibitor; PrEP = pre-exposure prophylaxis; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TFV = tenofovir

Table 6b. Other Initial Antiretroviral Regimens for Certain Clinical Scenarios

Several antiretroviral regimens are found to be effective and tolerable as initial regimens but have some disadvantages or have fewer supporting data from randomized clinical trials compared with the recommended regimens listed in Table 6a. However, one of these regimens may be preferred for an individual with HIV in certain clinical situations (also see Table 7). These regimens are listed below.

Type of Regimen	ARV Regimen	For Certain Clinical Scenarios	Other Considerations
INSTI Plus Two NRTIs	DTG/ABC/3TC (BI) (if HLA-B*5701-negative)	When concern about renal- or bone-associated AEs precludes the use of TDF or TAF	Test for HLA-B*5701 before prescribing ABC; do not prescribe if HLA-B*5701-positive. Consider avoiding ABC for people with multiple CV risk factors or known CV disease. Do not use in people with HBV coinfection unless an HBV-active drug, such as entecavir, TAF, or TDF is also used. Do not use following exposure to CAB-LA unless INSTI genotype shows sensitivity.
Boosted PI Plus Two NRTIs	(DRV/c[a] or DRV/r) plus (TAFor TDF[b]) plus (FTC or 3TC) (BI)	To avoid an INSTI-based regimen (e.g., documented INSTI resistance).	Assess for potential RTV- or COBI-related DDIs.
	(DRV/c[a] or DRV/r) plus ABC/3TC (BII) (if HLA-B*5701-negative)	To avoid an INSTI-based regimen (e.g., with suspected or documented INSTI resistance), *and* When concern about renal or bone-associated AEs precludes the use of TDF or TAF	Test for HLA-B*5701 before prescribing ABC; do not prescribe if HLA-B*5701-positive. Consider avoiding ABC for people with multiple CV risk factors or known CV disease. Do not use in people with HBV coinfection unless used with an HBV-active drug other than 3TC. Assess for potential RTV- or COBI-related DDIs.
NNRTI Plus Two NRTIs	DOR/TDF/3TC[b] (BI) or DOR plus TAF/FTC[b] (BIII)	To avoid an INSTI-based regimen (e.g., with suspected or documented INSTI resistance), *and* To avoid a PI-based regimen (e.g., with significant DDIs with concomitant medications)	

Table 6b. Other Initial Antiretroviral Regimens for Certain Clinical Scenarios

Type of Regimen	ARV Regimen	For Certain Clinical Scenarios	Other Considerations
	RPV/TAF/FTC (BII) Only if HIV RNA <100,000 copies/mL and CD4 count >200 cells/mm^3	To avoid an INSTI-based regimen (e.g., with suspected or documented INSTI resistance), *and* To avoid a PI-based regimen (e.g., with significant DDIs with concomitant medications), *and* When a single-tablet regimen containing an NNRTI and TAF is desired	Cannot take with PPI; space apart from H2 antagonist. Needs to be taken with a meal.
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] COBI should be avoided in pregnancy because lower concentrations of COBI and DRV have been observed during the second and third trimesters. For further information, refer to the Perinatal Guidelines.

[b] TAF and TDF are two forms of TFV approved by the U.S. Food and Drug Administration. 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, DOR/TDF/3TC, DRV/c, DRV/c/TAF/FTC, DTG/ABC/3TC, RPV/TAF/FTC, TAF/FTC, TDF/3TC, and TDF/FTC.

Key: 3TC = lamivudine; ABC = abacavir; AE = adverse event; ARV = antiretroviral; CD4 = CD4 T lymphocyte; COBI = cobicistat; CV = cardiovascular; DDI = drug–drug interaction; DOR = doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; FTC = emtricitabine; H2 = histamine type 2; 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; PPI = proton pump inhibitor; RPV = rilpivirine; RTV = ritonavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TFV = tenofovir

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

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This table guides clinicians in choosing an initial antiretroviral (ARV) regimen according to various patient and regimen characteristics and specific clinical scenarios. ARV drugs/regimens that are listed in Table 6a as *Recommended Initial Regimens for Most People With HIV* and in Table 6b as *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios* are included in this table (see Initial Combination Antiretroviral Regimens for People With HIV). 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. Please see Table 9 for additional information regarding the advantages and disadvantages of particular ARV medications recommended to be used as initiation therapy.

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
Pre-ART Characteristics	CD4 count <200 cells/mm^3	Do not use RPV-based regimens.	Higher rates of virologic failure have 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 RPV-based regimens.	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/TAF/FTC • 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 is a potentially fatal reaction that is highly associated with the HLA-B*5701 allele.
	Prior exposure to oral TDF/(3TC or FTC) or TAF/3TC PrEP	Use DTG or BIC plus two NRTIs. DTG/3TC could be considered if testing confirms no 3TC resistance mutations.	DTG/3TC should be avoided if resistance testing results are not available, as presence of 3TC resistance mutations may lead to use of DTG monotherapy.
	Prior exposure to CAB-LA for PrEP	INSTI genotype resistance testing should be performed. If INSTI Resistance Is Present or If ART Needs to Be Started Before Genotype Test 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 INSTI-resistant virus.

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

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
		If No INSTI Resistance Is Identified • BIC/TAF/FTC, *or* • DTG plus (TAF or TDF)[a] plus (3TC or FTC)	
	People with no prior exposure to CAB-LA for PrEP and ARV regimen should be started rapidly and before HIV drug resistance results are available.	Avoid ABC, DTG/3TC, and NNRTI-based regimens. Use • BIC/TAF/FTC, *or* • DTG plus (TAF or TDF)[a] plus (3TC or FTC) In People Who Used INSTI-Based ART for PEP Post-exposure Prophylaxis or Who Are Suspected to Have Acquired HIV From Someone Failing an INSTI-Based Regimen • Obtain INSTI genotypic resistance test and start one of the following regimens: o BIC/TAF/FTC, *or* o DTG plus (TAF or TDF)[a] plus (3TC or FTC)	Transmitted mutations conferring NNRTI and NRTI resistance are more likely than mutations associated with PI or INSTI resistance. HLA-B*5701 results may not be available rapidly; thus, ABC is not recommended. Because of the current low rates of transmitted INSTI resistance in the United States, even when there is suspicion that HIV was acquired from a partner with virologic failure while on an INSTI, an INSTI-based regimen can be started, pending the results of the INSTI genotype.
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 • RPV/TAF/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 without another HBV agent. Do not use RPV/TAF/FTC if HIV RNA is >100,000 copies/mL and CD4 count is <200 cells/mm^3.
	Food effects	Regimens That Can Be Taken Without Regard to Food • BIC-, DOR-, or DTG-based regimens	Oral bioavailability of these regimens is not significantly affected by food.
		Regimens That Should Be Taken With Food	Food improves absorption of

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

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
		• DRV/r- or DRV/c-based regimens • RPV/TAF/FTC	these regimens. RPV-containing regimens should be taken with ≥390 calories of food.
Presence of Other Conditions	Chronic kidney disease (defined as CrCl <60 mL/min)	In general, avoid TDF. For patients with progressively declining renal function, consider avoiding all TFV-containing (TAF or TDF) regimens. Refer to Appendix B, Table 12 for specific ARV drug dosing recommendations in patients with renal impairment.	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. TAF has less impact on renal dysfunction than TDF. 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. Patients with cirrhosis should be carefully evaluated by an expert in advanced liver disease.
	Concern for 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 increase than others.	Reasons for differences in weight gain among ART regimens are unknown. Note: Weight gain should not be a reason to avoid taking an INSTI-based regimen.
	Osteoporosis	Avoid TDF.[a]	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 RPV-based regimens.	RPV can exacerbate psychiatric symptoms and may

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

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
		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.	be associated with suicidality. Some 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, 24d, and 24g) for dosing recommendations when drugs used for psychiatric illnesses are used with certain ARVs.
	Cardiac QTc interval prolongation	Consider avoiding 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 RPV concentrations may cause QTc prolongation.
	High risk for CV events	Consider avoiding ABC-based regimens. 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, but not all, studies. Certain ARV regimens are associated with more favorable lipid profiles than other regimens.
	Hyperlipidemia	PI/c and PI/r have been associated with hyperlipidemia. BIC, DOR, DTG, and RPV have fewer lipid effects.	TDF has been associated with lower lipid levels than ABC or TAF.
	Patients with history of poor adherence to 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.	

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

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
Presence of Coinfections	HBV infection	**Avoid regimens** that do not contain NRTIs. 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).	TDF, TAF, FTC, and 3TC are active against both HIV and HBV. 3TC- or FTC-associated HBV resistance mutations can emerge 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.	
	Concomitant use with rifamycin antibiotics (e.g., rifabutin, rifampin, and rifapentine)	Recommended regimens may require dose adjustment. See the drug–drug interaction tables (Tables 24a, 24b, 24c, 24d, 24e, 24f, 24g, 25a, and 25b) 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 U.S. Food and Drug Administration–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; BIC = bictegravir; BMD = bone mineral density; CAB-LA = long-acting cabotegravir; CD4 = CD4 T lymphocyte; CrCl = creatinine clearance; CV = cardiovascular; CYP = cytochrome P; DOR = doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; FTC = emtricitabine; HBV = hepatitis B virus; HCV = hepatitis C virus; HLA = human leukocyte antigen; INSTI = integrase strand transfer inhibitor; 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; PEP = post-exposure prophylaxis; PrEP = pre-exposure prophylaxis; QTc = QT corrected for heart rate; RPV = rilpivirine; RTV = ritonavir; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TFV = tenofovir; UGT = uridine diphosphate glucuronosyltransferase

Table 8a. Characteristics of Nucleoside Reverse Transcriptase Inhibitor Options for People Without Prior Antiretroviral Treatment

Note: Listed in order of the Panel's recommendations in Tables 6a and 6b.

Characteristics	TAF/FTC	TDF/FTC	TDF/3TC	3TC	ABC/3TC
Dosing Frequency	Once daily	Once daily	Once daily	Once daily	Once daily
Available Coformulations for People Without Prior ARV Treatment	• TAF 25 mg/FTC • BIC/TAF 25 mg/FTC • DRV/c/TAF 10 mg/FTC • RPV/TAF 25 mg/FTC	• TDF/FTC	• TDF/3TC • DOR/TDF/3TC	• DTG/3TC	• ABC/3TC • DTG/ABC/3TC
Adverse Effects	TAF • Renal insufficiency, proximal renal tubulopathy (less frequent than with TDF) • Decrease in BMD (less than with TDF)	TDF • Renal insufficiency, proximal renal tubulopathy • Decrease in BMD • Renal and bone toxicity are exacerbated by pharmacologic boosters.	TDF • Renal insufficiency, proximal renal tubulopathy • Decrease in BMD • Renal and bone toxicity are exacerbated by pharmacologic boosters.	3TC • No notable adverse effects	ABC • HSR to ABC is associated with the presence of HLA-B*5701 allele.[b] • Increase in CV events is associated with ABC use in some but not all cohort studies.
Other Considerations	• Also used for HBV treatment. Discontinuation may precipitate HBV flare. • See Appendix B, Table 11 for dosing recommendations in people with renal insufficiency. • Some studies reported less weight gain and lower LDL, HDL, TC, and triglycerides with TDF than with TAF.			• 3TC or ABC/3TC should not be used as treatment for HBV without adding another HBV-active drug.	

[a] 3TC is recommended for use with DTG in some people as initial ART. See Table 6a and the discussion below for more information. Otherwise, dual-NRTI backbones are recommended.

[b] Perform HLA-B*5701 testing before initiating ABC; if result is positive, do not start ABC and add ABC to patient's allergy list. See the HLA-B*5701 Screening section for more information.

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; BIC = bictegravir; BMD = bone mineral density; CV = cardiovascular; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DTG = dolutegravir; FTC = emtricitabine; HBV = hepatitis B virus; HDL = high-density lipoprotein; HLA = human leukocyte antigen; HSR = hypersensitivity reaction; LDL = low-density lipoprotein; NRTI = nucleoside reverse transcriptase inhibitor; RPV = rilpivirine; TAF = tenofovir alafenamide; TC = total cholesterol; TDF = tenofovir disoproxil fumarate

Table 8b. Characteristics of Integrase Strand Transfer Inhibitors That Are Recommended as Part of Initial Antiretroviral Therapy

	BIC	DTG
Dosing Frequency	Once daily	Once Daily • As initial ART or in people with no INSTI-resistance mutations Twice Daily • If used with certain CYP3A4 and UGT1A1 inducers; *or* • In people with certain INSTI drug resistance mutations
STR Available as Initial ART	BIC/TAF/FTC	• DTG/ABC/3TC • DTG/3TC
Available as a Single Drug Tablet	No	Yes
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
Adverse Reactions	• ↑ CPK 4% • CNS side effects were rarely reported in clinical trials. • Diarrhea, nausea, and headache may occur in some cases.	• ↑ CPK, myositis • CNS side effects such as insomnia and headache have been reported; depression and suicidality are rare, occurring primarily in people with preexisting conditions. • Hypersensitivity, hepatotoxicity
CYP3A4 Drug–Drug Interactions	CYP3A4 substrate	CYP3A4 substrate (minor)
Chelation With Polyvalent Cation Supplements and Antacids	Oral absorption may be reduced by polyvalent cations. See Table 24d for recommendations regarding dosing separations and these drugs.	
Other Key Potential Drug Interaction Mechanisms	P-gp substrate, UGT1A1 substrate, OCT2 and MATE1 inhibitor	P-gp substrate, UGT1A1 substrate
Other Factors	Both BIC and DTG decrease tubular secretion of creatinine without affecting glomerular function. This may result in an increase in serum creatinine of approximately 0.1–0.2 mg/dL.	

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; BIC = bictegravir; CNS = central nervous system; CPK = creatine phosphokinase; CYP = cytochrome P450; DTG = dolutegravir; EVG = elvitegravir; FTC = emtricitabine; INSTI = integrase strand transfer inhibitor; MATE1 = multidrug and toxic compound extrusion 1; OCT2 = organic cation transporter 2; P-gp = p-glycoprotein; RAL = raltegravir; STR = single-tablet regimen; TAF = tenofovir alafenamide; UGT = uridine diphosphate glucuronosyltransferase

Table 8c. Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors That Are Recommended as Initial Antiretroviral Therapy in Certain Clinical Scenarios

Characteristics	DOR	RPV[a]
Dosing Frequency	Once daily	Once daily
Food Requirement	With or without food	With a meal
STR Available as Initial ART Recommended in Table 6b	DOR/TDF/3TC	RPV/TAF/FTC
Available as a Single-Drug Tablet	Yes	Yes
Adverse Effects	Generally well tolerated	• Depression • Headache • Skin rash • QTc prolongation
CYP3A4 Drug–Drug Interactions	CYP3A4 substrate	CYP3A4 substrate
Other Significant Drug Interactions	None	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 an 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; CYP = cytochrome P; DOR = doravirine; 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 as Initial Antiretroviral Therapy in Certain Clinical Scenarios

Characteristic	DRV
Dosing Frequency	Once daily for persons with no prior PI experience.
PK Boosting	DRV should only be used with a PK booster (i.e., RTV or COBI).
Fixed-Dose Formulation	• DRV/c • DRV/c/TAF/FTC
Available as a Single-Drug Tablet	Yes
Adverse Effects	• Skin rash • Increase in serum transaminase • Hyperlipidemia • Diarrhea, nausea
CYP3A4 Drug–Drug Interactions	CYP34A substrate, inhibitor
Other Significant Drug Interactions	N/A

Key: COBI = cobicistat; CYP = cytochrome P; DRV = darunavir; DRV/c = darunavir/cobicistat; FTC = emtricitabine; N/A = not applicable; PI = protease inhibitor; PK = pharmacokinetic; RTV = ritonavir; TAF = tenofovir alafenamide

Table 9. Advantages and Disadvantages of Antiretroviral Components of Initial Antiretroviral Therapy Listed in Table 6a and Table 6b

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Note: All drugs within an ARV class are listed in alphabetical order. Information based on Table 6a and Table 6b in the Initial Combination Antiretroviral Regimens for People With HIV section.

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 people who test positive for the HLA-B*5701 allele. As a result, HLA-B*5701 testing is required before use. • 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, or RPV • Active against HBV; a recommended dual-NRTI option for people with HBV/HIV coinfection • Smaller decline in renal function, less proteinuria, and smaller reductions in BMD than TDF/FTC • Approved for people with eGFR ≥30 mL/min • Can be used in people on chronic hemodialysis	• See text in the NRTI section regarding weight gain with TAF.
	TDF/3TC	• Coformulated with DOR • Generic formulations are available for TDF, 3TC, or TDF/3TC. • Long-term clinical experience • Active against HBV	• Renal toxicity, including proximal tubulopathy and acute or chronic renal insufficiency, especially when combined with pharmacologic boosters • Osteomalacia has been reported as a consequence of proximal tubulopathy. • Decreased BMD has been associated with use of TDF, especially when combined with pharmacologic boosters.
	TDF/FTC	• Active against HBV; a recommended dual-NRTI option for people with HIV/HBV coinfection • TDF is associated with lower lipid levels than TAF.	• Renal toxicity, including proximal tubulopathy and acute or chronic renal insufficiency, especially when combined with pharmacologic boosters • Osteomalacia has been reported as a consequence of proximal tubulopathy. • Decreased BMD has been associated with use of TDF, especially when combined with pharmacologic boosters.

Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy Listed in Table 6a and Table 6b

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
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 unless on another HBV active drug, 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. • CYP3A4 and UGT1A1 substrate (but not a CYP3A4 inducer or inhibitor); potential for drug–drug interactions. • See text in the INSTI section regarding weight gain and INSTI use.
	DTG	• Higher barrier to resistance than EVG or RAL • Coformulated with ABC/3TC and 3TC as STR • 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. • UGT1A1 substrate; potential for drug interactions (see Table 24d) • Depression and suicidal ideation (rare; usually in people with preexisting psychiatric conditions) • See text in the INSTI section regarding weight gain and INSTI use.
NNRTI	DOR	• Coformulated with TDF/3TC • Fewer CNS side effects compared to EFV and RPV • No food requirement	• Shorter-term clinical experience than with RPV • Potential for CYP450 drug interactions (see Tables 24b, 25a, and 25b) • Treatment-emergent DOR resistance mutations may confer resistance to certain NNRTIs.
	RPV	• Coformulated with TAF/FTC	• Not recommended in people 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 people. • Depression and suicidality • QTc interval prolongation; consider using an alternative to RPV in people 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

Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy Listed in Table 6a and Table 6b

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
			PIs and INSTIs. • More NNRTI-, TDF-, and 3TC-associated mutations at virologic failure than with regimens that contain EFV and two 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).
PI	DRV/c or DRV/r	• Higher barrier to resistance than NNRTIs • 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[a] • Hepatotoxicity has been reported, especially in those with preexisting liver disease.
	DRV/c Specific considerations	• Coformulated as DRV/c and DRV/c/TAF/FTC	• COBI inhibits active tubular secretion of Cr and can increase serum Cr without affecting renal glomerular function. • Coadministration with TDF is not recommended in people 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.

[a] D:A:D international prospective multicohort study[1]

Key: 3TC = lamivudine; ABC = abacavir; Al = aluminum; ART = antiretroviral therapy; ARV = antiretroviral; 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/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; eGFR = estimated glomerular filtration rate; FTC = emtricitabine; GI = gastrointestinal; H2 = histamine 2; HBV = hepatitis B virus; HLA = human leukocyte antigen; HSR = hypersensitivity reaction; INSTI = integrase strand transfer inhibitor; Mg = magnesium; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PK = pharmacokinetic; PPI = proton pump inhibitor; QTc = QT corrected for heart rate; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; UGT = uridine diphosphate glucuronosyltransferase

Table 10. Antiretroviral Options for People With HIV and Virologic Failure

Designing a new regimen for people with HIV 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 people 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 before and after regimen changes.

Clinical Scenario	Type of Failing Regimen	Resistance Considerations	New Regimen Options[a]	Goal
First Regimen Failure	NNRTI plus two NRTIs	Most likely resistant to NNRTI +/– 3TC or FTC (i.e., NNRTI mutations +/– M184V/I).[b] Additional NRTI mutations also may be present.	DTG (or possibly BIC) plus two NRTIs (preferably at least one fully active[c]) (AI); *or* Boosted PI plus two NRTIs (preferably at least one fully active) (AI); *or* Boosted PI plus INSTI (boosted DRV plus DTG [AI]; LPV/r plus RAL [CI])	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)[b]	DTG, or possibly BIC, plus two NRTIs (preferably at least one fully active; if only one of the NRTIs is fully active[c] or if adherence is a concern, DTG is currently preferred over other INSTIs) (AIII); *or* Continue same regimen (AII); *or* Boosted PI plus INSTI (boosted DRV plus DTG [AI]; LPV/r plus RAL [CI]); *or* Another boosted PI plus two NRTIs (at least one fully active[c]) (AIII).	Resuppression
	INSTI plus two NRTIs	If failure with no INSTI resistance	Boosted PI plus two NRTIs (preferably at least one fully active[c]) (AIII); *or* DTG, or likely BIC, plus two NRTIs (preferably at least one fully active[c]) (AIII); *or* DRV/r plus DTG (AIII)	Resuppression
		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[c]) (AIII); *or* DTG[d] twice daily or possibly BIC (if HIV is sensitive) plus two fully active NRTIs (BIII); *or* DTG[d] twice daily or possibly BIC (if HIV is sensitive) plus a boosted PI	Resuppression

Table 10. Antiretroviral Options for People with HIV and Virologic Failure

Clinical Scenario	Type of Failing Regimen	Resistance Considerations	New Regimen Options[a]	Goal
			(preferably DRV/r) (AIII).	
	INSTI plus NNRTI (DTG/RPV or LA CAB/RPV)	INSTI and/or NNRTI resistance possible	Use ART history and past and current resistance testing to design a new regimen. Consult an expert in drug resistance as needed.	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 fewer than three fully active drugs, include as many fully active drugs as possible, along with potentially partially active drugs (BII). Consider enrollment into clinical trials or expanded access programs for investigational agents if available. Discontinuation of all ARV drugs is not recommended (AI).	Resuppression if possible; otherwise, keep viral RNA levels as low as possible and CD4 count as high as possible.
People 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 person 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

Table 10. Antiretroviral Options for People with HIV and Virologic Failure

[a] When switching an ARV regimen in a person with HBV/HIV coinfection, ARV drugs that are active against HBV and have a high resistance barrier to HBV (i.e., tenofovir) should be continued as part of the new regimen, or another HBV drug (i.e., entecavir) should be started. Discontinuation of these drugs may lead to the reactivation of HBV, which may result in serious hepatocellular damage.

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

[c] See text for details and additional options in special settings.

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

Key: 3TC = lamivudine; ART = antiretroviral therapy; ARV = antiretroviral; BIC = bictegravir; CD4 = CD4 T lymphocyte; DRV = darunavir; DRV/r = darunavir/ritonavir; 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 11. 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 12: 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 12: 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 13: 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.

Table 13: AYA With HIV ARV Adherence Barriers and Strategies to Support Adherence

ART Adherence Barrier	Adherence Support Strategy	Rationale for Adherence Support Strategy
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.
	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 13: 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 14. 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 people with the signs, symptoms, or laboratory findings described below and in asymptomatic people with a possible acute (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 someone who has HIV or is at risk of HIV infection, sharing needles, syringes, or equipment for drug preparation or injection, or any situation where a person's mucous membranes or broken skin come into contact with bodily fluids that may carry 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 or 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, prevent HIV transmission (AII), and preserve immune function (AIII).
- All people 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.
- Standard genotypic drug-resistance testing should be performed for mutations in the reverse transcriptase and protease genes (AIII) for all people with early HIV. Genotype testing for INSTI resistance should be performed for those who acquire HIV during or after the use of CAB-LA as PrEP, if transmitted INSTI resistance is suspected, or if HIV diagnosis is made after receiving an INSTI-based regimen for PEP (AIII).

Table 14. Identifying, Diagnosing, and Treating Acute and Recent HIV Infection

- 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):
  - BIC/TAF/FTC (AIII); or
  - DTG with (TAF or TDF)[b] plus (FTC or 3TC) (AIII)
- For individuals with a history of using CAB-LA as PrEP, genotypic resistance testing performed before starting ART should include screening for INSTI-resistance mutations (AIII). Recommended regimens include the following:
  - (DRV/c[c] or DRV/r) 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 acquire HIV during the use of CAB-LA and possibly up to 4 years after.

[a] In some settings, activities that increase the risk of HIV infection may not be recognized or perceived as risky by the health care provider, the person at risk, or both. Thus, even in the absence of reported high-risk activities, 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.

[c] COBI should be avoided in pregnancy because lower concentrations of COBI and DRV have been reported during the second and third trimesters.

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

Table 15. 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 people with CrCl 30–50 mL/min	No significant interaction with ARV drugs expected.	Contraindicated in people 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 people 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 AUD.
Opioid Use Disorder			
Buprenorphine	Individualize buprenorphine dosing based on the person'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 person 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. People 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	The FDA has approved a wide variety of nicotine replacement products. All formulations are effective.	No significant interaction with ARV drugs expected.	Work with the person to identify the route of delivery that they will use and find most helpful.

Table 15. Medications for Treatment of Substance Use Disorders

Medication	Dose and Recommendations	Potential Interaction With ARV Drugs	Comments
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.	For optimal results, tobacco quit date should occur 1 week after starting therapy.
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 people with CrCl <30 mL/min.	No significant interaction with ARV drugs expected.	For optimal results, tobacco quit date should occur 1 week after starting therapy.

Key: ARV = antiretroviral; AUD = alcohol use disorder; CrCl = creatinine clearance; CYP = cytochrome P450; FDA = U.S. Food and Drug Administration; FPV = fosamprenavir; LPV/r = lopinavir/ritonavir; OTP = opioid treatment program; OUD = opioid use disorder; PO = orally; QTc = QT corrected for heart rate; RTV = ritonavir

Table 16a. Common Gender-Affirming Hormone Therapies

Feminizing Drugs		Physical Effects
Estrogens	Estradiol, PO 17 β-Estradiol, transdermal (patch) Estradiol valerate, IM Estradiol cypionate, IM	Redistribution of body fat Breast growth Decrease in muscle mass and strength Softening of skin Decrease in spontaneous erection
Androgen Blockers	Mineralocorticoid Receptor Antagonist • Spironolactone, PO 5α-Reductase Inhibitors • Dutasteride, PO • Finasteride, PO • Cyproterone acetate, PO* GnRH Agonists • Leuprolide, IM • Triptorelin, IM or SC • Goserelin, SC	
Masculinizing Drugs		**Physical Effects**
Testosterones	Testosterone enanthate, IM or SC Testosterone cypionate, IM or SC Testosterone undecanoate, IM Testosterone gel, transdermal	Fat redistribution Facial/body hair growth Deepening of voice Increased muscle mass Amenorrhea Vaginal atrophy Clitoral enlargement

* Not available in the United States

Key: GnRH = gonadotropic hormone-releasing hormone; IM = intramuscular; PO = oral; SQ = subcutaneous

Table 16b. Potential Interactions Between Common Gender-Affirming Hormone Therapies and Antiretroviral Drugs*

Potential Effect on GAHT Drugs	ARV Drugs	GAHT Drugs That May be Affected by ARV Drugs	Clinical Recommendations and Other Considerations for GAHT or ARV Drugs
ARV Drugs With the Least Potential to Impact GAHT Drugs	All NRTIs Entry Inhibitors • IBA, MVC, T-20 INSTIs (unboosted) • BIC, CAB (IM or PO), DTG, RAL NNRTIs • DOR, RPV (IM or PO)	None	No dose adjustments necessary. Titrate dose based on desired clinical effects and hormone concentrations. Note: Avoid IM buttock injections into sites with gluteal implants and/or soft tissue fillers.
ARV Drugs That May Increase Concentrations of Some GAHT Drugs	• EVG/c • PI/c, PI/r • LEN	Dutasteride Finasteride Testosterone	Monitor 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 Some GAHT Drugs	PI/r NNRTIs • EFV, ETR	Estradiol	Increase the dose of estradiol as needed to achieve the desired clinical effects and hormone concentrations.
	NNRTIs • EFV, ETR	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 Some 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, 24e, 24f, and 24g for additional information regarding drug–drug interactions between ARV drugs and gender-affirming medications.

* Only ARV drugs commonly used in clinical practice in the United States are included in this table.

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

Table 17a. Drug Interactions Between Antiretroviral Drugs and Immunosuppressants Used Post-Transplant

	Overview of Interaction Potential	Tacrolimus	Sirolimus	Cyclosporine
NRTI	↔ NRTI ↔ Immunosuppressant	Initiate standard doses. Monitor renal function if used with TDF.	Initiate standard doses. Monitor renal function if used with TDF.	Initiate standard doses. Monitor renal function if used with TDF.
NNRTI	↔ NNRTI With EFV, ETR, and NVP • ↓ Immunosuppressant expected With DOR (A Weak Inducer) • ↓ Immunosuppressant possible With RPV • ↔ Immunosuppressant	Initiate standard doses and adjust based on TDM. With EFV, ETR, and NVP • May need higher doses With RPV • Monitor QTc with RPV.	Initiate standard doses and adjust based on TDM. With EFV, ETR, and NVP • May need higher doses With RPV • Monitor QTc with RPV.	Initiate standard doses and adjust based on TDM. With EFV, ETR, and NVP • May need higher doses. With RPV • Monitor QTc with RPV.
PI (With COBI or RTV as PK Booster)	↔ PI ↑ Immunosuppressant requiring dose reduction and/or extending dosing interval	↑ ↑ Tacrolimus Switch to a non-PI/c or PI/r-based regimen. If not possible, consider initiating tacrolimus 0.5 mg PO every 5–7 days. Adjust based on TDM.	↑ ↑ Sirolimus Switch to a non-PI/c or PI/r-based regimen. If not possible, consider initiating sirolimus 1–1.5 mg PO once weekly. Adjust based on TDM.	↑ CsA Consider initiating reduced dose of CsA at 5% to 20% of standard daily dose. Adjust based on TDM.
INSTI	↔ INSTI For BIC, CAB, DTG, or RAL • ↔ Immunosuppressant With EVG/c • ↑ Immunosuppressant with EVG/c	For BIC, CAB, DTG, or RAL • Initiate standard doses and adjust based on TDM. With EVG/c • ↑ ↑ Tacrolimus expected • Switch to a non–EVG/c-based regimen. If not possible, consider initiating tacrolimus 0.5 mg PO every 5–7 days. Adjust	For BIC, CAB, DTG, or RAL • Initiate standard doses and adjust based on TDM. With EVG/c • ↑ ↑ Sirolimus expected • Switch to a non–EVG/c-based regimen. If not possible, consider initiating sirolimus 1–1.5 mg PO once weekly. Adjust based	For BIC, CAB, DTG, or RAL • Initiate standard doses and adjust based on TDM. With EVG/c • ↑ CsA expected • Consider initiating reduced CsA at 10% to 20% of total standard daily dose. Adjust based on TDM.

Table 17a. Drug Interactions Between Antiretroviral Drugs and Immunosuppressants Used Post-Transplant

	Overview of Interaction Potential	Tacrolimus	Sirolimus	Cyclosporine
		based on TDM.	on TDM.	
Capsid Inhibitors	↔ LEN expected ↑ Immunosuppressant expected	No data to guide dosing Adjust based on TDM.	No data to guide dosing Adjust based on TDM.	No data to guide dosing Adjust based on TDM.
CCR5 Antagonist, Fusion, Attachment, and Post-Attachment Inhibitors	↔ ARV drugs expected ↔ Immunosuppressant expected	Initiate standard doses. Adjust based on TDM.	Initiate standard doses. Adjust based on TDM.	Initiate standard doses. Adjust based on TDM.

Key: ↔ = No clinically significant change; ↓ = decreased; ↑ = increased; ↑ ↑ = greatly increased; ARV = antiretroviral; BIC = bictegravir; CAB = cabotegravir; CCR5 = chemokine co-receptor 5; COBI = cobicistat; CsA = cyclosporine; DOR = doravirine; DTG = dolutegravir; EFV= efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; INSTI = integrase strand transfer inhibitor; LEN = lenacapavir; NRTI = nucleos(t)ide reverse transcriptase inhibitor; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PI/c = cobicistat-boosted protease inhibitor; PI/r = ritonavir-boosted protease inhibitor; PO = orally; QTc = QT corrected for heart rate; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; TDF = tenofovir disoproxil fumarate; TDM = therapeutic drug monitoring

Table 17b. Drug Interactions Between Antiretroviral Drugs and Medications Commonly Used in Transplant Recipients

Drug Class	Examples	Effects of Interactions
Azole Antifungals	Isavuconazole Itraconazole Posaconazole Voriconazole	CYP Inhibition (e.g., With RTV or COBI as PK Booster, Azoles)[a] • ↑ Azole concentration, ↑ toxicities • ↑ ARV concentration possible, ↑ toxicities CYP or Glucuronidation Induction (e.g., EFV, NVP) • ↓ Azole concentration, ↓ efficacy
Chemotherapy	Busulfan Cyclophosphamide Etoposide[b]	CYP Inhibition or Induction (e.g., With RTV or COBI as PK Booster) • ↑ or ↓ Chemotherapy concentration with RTV, ↑ toxicities, or ↓ efficacy • ↑ Chemotherapy concentration with COBI, ↑ toxicities CYP Induction (e.g., EFV, ETR, NVP) • ↓ Chemotherapy concentration, ↓ efficacy
Corticosteroids	Dexamethasone	Dose-Dependent CYP3A4 Induction • ↓ ARVs that are metabolized by CYP3A4
	High-dose Prolonged Use Prednisone/Prednisolone	CYP3A4 Inhibition (e.g., With RTV or COBI as PK booster) • ↑ Steroid concentration, ↑ toxicities
Acid-Reducing Medications	PPI, H2 Antagonists	Increase in Gastric pH • ↓ Absorption of certain ARVs, including ATV or RPV. See Table 24a and 24b for recommended timing of administration if concomitant therapy is needed.

Key: ARV = antiretroviral, ATV = atazanavir; COBI = cobicistat; CYP = cytochrome P450; CYP3A4 = cytochrome P3A4; EFV = efavirenz; ETR = etravirine; H2 = histamine 2; NVP = nevirapine; PK = pharmacokinetic; PPI = proton pump inhibitor; RPV = rilpivirine; RTV = ritonavir

[a] CYP inhibition by azoles can ↑ concentrations of immunosuppressants and certain cancer chemotherapy drugs.

[b] The listed are frequently used conditioning therapy pre-hematopoietic transplants that have potential interactions with ART. For other chemotherapeutic agents, consult a clinical pharmacist with expertise in transplant-related drug–drug interactions.

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	✓	✓	✓	✓	✓	✓

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
DTG	✓	✓ If used with TDF, monitor for TDF-associated adverse events.	✓	✓	✓	✓
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.

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

[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
? = 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 person-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 an individual's knowledge about HIV, HIV prevention, and HIV treatment and provide information based on this assessment.	• Keeping the 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 the importance of staying in HIV care.
Identify facilitators, potential barriers to adherence, and necessary medication management skills both when starting ART and thereafter.	• Assess each individual's cognitive competence and impairment. • Assess behavioral and psychosocial challenges, including mental illnesses, trauma, social support levels, alcohol consumption, 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, Pharmaceutical Company HIV Patient Assistance Programs and Cost-Sharing Assistance Programs). • Assist people during insurance enrollment periods to facilitate enrollment in plans that cover antiretrovirals. • Provide resources about stable housing, social support, transportation assistance, 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 people with HIV 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 a regimen to predictable and routine daily events. • Consider preferential use of ART regimen with a high barrier to resistance, such as BIC-, DTG-, or boosted DRV-based ART if poor adherence is anticipated. • Consider the use of STR or fixed-dose-combination formulations to reduce pill burden and/or dosing frequency. • Consider the use of LA CAB/RPV if clinically appropriate (see the Long-Acting Antiretroviral Therapy section above for further discussion). • 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 biological 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 people of the benefits of low or nondetectable levels of HIV viral load (e.g., "Undetectable = Untransmittable") and increases in CD4 counts. • Thank people for attending their appointments.
Identify the type of and reasons for poor adherence and target ways to improve adherence.	Identify if any of the following have contributed to poor 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. • Appointment reminders and incorporation of input from people with HIV in appointment scheduling. • Cost-related issues (e.g., copays for medications or visits, missed work time). • Mental illness, 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 prescription assistance programs (see "Provide needed resources" above in this table). • Use motivational interviews. • Provide outreach for people who drop out of care. • Use peer or paraprofessional treatment navigators. • Recognize positive clinical outcomes resulting from better adherence. • Arrange for DOT for people in substance use treatment (if feasible). • Enhance clinic support and structures to promote linkage and retention (e.g., reminder calls, flexible scheduling, assessment of clinic service 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; DRV = darunavir; DTG = dolutegravir; LA CAB/RPV = long-acting cabotegravir/rilpivirine; 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

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

Adverse Effect	Drug Class					
	NRTIs	NNRTIs	PIs	INSTIs	EIs	CI
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 medications that may cause PR prolongation.	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 of medications that may prolong QTc interval.	N/A
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

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

Adverse Effect	Drug Class					
	NRTIs	NNRTIs	PIs	INSTIs	EIs	CI
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
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
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	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

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

Adverse Effect	Drug Class					
	NRTIs	NNRTIs	PIs	INSTIs	EIs	CI
		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				
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.

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	
Dyslipidemia Hypertriglyceridemia (with or without elevated LDL level)	RTV- or COBI-boosted PI, EFV-based regimens	INSTI, DOR, or RPV	Elevated TG and LDL levels are more common with LPV/r and FPV/r than with other RTV-boosted PIs. Improvements in TG and LDL levels have been observed with switch from LPV/r to ATV or ATV/r.[c]
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	PI- or INSTI-based regimen	Mild rashes that develop after initiation of NNRTIs other than NVP rarely require treatment switch. When serious rash develops due to any NNRTI, switch to another drug

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	
	NVP and EFV)		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, although caps on out-of-pocket spending for drugs covered under Medicare Part D went into effect in 2024; 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.

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

Insurance/Health Program	Prescription Drug Pricing and Access
Veterans Affairs	The FCP is the maximum price manufacturers may charge the four largest federal purchasers of pharmaceuticals (the "Big Four"): the U.S. 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.
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 antiretroviral (ARV) drugs[a] as a general reference for health care providers when considering the cost of HIV treatment. Health care providers should contact pharmacies or payers regarding actual prices, comparative cost savings, formulary restrictions, and cost-sharing requirements. The wholesale acquisition cost (WAC) is the list price published by manufacturers for prescription drugs or biologics sold to wholesalers. The WAC price approximates what retail pharmacies pay wholesalers for single-source (e.g., brand-name) drugs. There is a range of WAC prices for generic ARV drugs 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. Average wholesale price (AWP) has historically been used as the basis for setting public (e.g., Medicaid) and private (e.g., commercial insurer) reimbursement rates for pharmacies. Neither WAC nor AWP 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 AIDS Drug Assistance Programs. The availability of these discounts and rebates depends on product demand, market competition, and WAC price increases set by manufacturers. Maximum 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 federal upper limit (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 state maximum allowable costs and commercial insurers set their own reimbursement upper limits with pharmacies. While 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 required competition.

ARV Drug (Generic and Brand Names)	Strength, Formulation	Capsules, mLs, Tablets, or Vials	Wholesale Acquisition Cost[b]	Average Wholesale Price[b]	Federal Upper Limit (As of July 31, 2024)[c]
		(Monthly Values, Unless Otherwise Noted)			
NRTIs					
Abacavir					
Generic	300-mg tablet	60 tablets	$100 to $150	$578 to $603	$48
Ziagen	300-mg tablet	60 tablets	$559	$670	N/A
Emtricitabine					
Generic	200-mg capsule	30 capsules	$390 to $464	$482 to $579	Pending

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

ARV Drug (Generic and Brand Names)	Strength, Formulation	Capsules, mLs, Tablets, or Vials	Wholesale Acquisition Cost[b]	Average Wholesale Price[b]	Federal Upper Limit (As of July 31, 2024)[c]
		(Monthly Values, Unless Otherwise Noted)			
Emtriva	200-mg capsule	30 capsules	$537	$644	N/A
Lamivudine					
Generic	300-mg tablet	30 tablets	$40 to $415	$429	$39
Epivir	300-mg tablet	30 tablets	$416	$499	N/A
Tenofovir Disoproxil Fumarate					
Generic	300-mg tablet	30 tablets	$27 to $300	$167 to $1,216	$42
Viread	300-mg tablet	30 tablets	$1,254	$1,504	N/A
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	$100 to $302	$1,393 to $1,395	$40
Tenofovir Alafenamide/Emtricitabine					
Descovy	25-mg/200-mg tablet	30 tablets	$2,202	$2,643	N/A
Tenofovir Disoproxil Fumarate/Emtricitabine					
Generic	300-mg/200-mg tablet	30 tablets	$25 to $420	$70 to $2,100	$15
Truvada	300-mg/200-mg tablet	30 tablets	$1,842	$2,211	N/A
Tenofovir Disoproxil Fumarate/Lamivudine					
Cimduo	300-mg/300-mg tablet	30 tablets	$1,185	$1,422	N/A
Zidovudine/Lamivudine					
Generic	300-mg/150-mg tablet	60 tablets	$125 to $578	$265 to $932	$44

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

ARV Drug (Generic and Brand Names)	Strength, Formulation	Capsules, mLs, Tablets, or Vials	Wholesale Acquisition Cost[b]	Average Wholesale Price[b]	Federal Upper Limit (As of July 31, 2024)[c]
		(Monthly Values, Unless Otherwise Noted)			
NNRTIs					
Efavirenz					
Generic	600-mg tablet	30 tablets	$80 to $894	$1,043 to $1,118	$55
Doravirine					
Pifeltro	100-mg tablet	30 tablets	$1,760	$2,112	N/A
Etravirine					
Generic	200-mg tablet	60 tablets	$1,287	$1,609	$878
Intelence	200-mg tablet	60 tablets	$1,469	$1,762	N/A
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	N/A
Rilpivirine					
Edurant	25-mg tablet	30 tablets	$1,483	$1,780	N/A
PIs					
Atazanavir					
Generic	200-mg capsule	60 capsules	$178 to $316	$1,502 to $1,668	$711
Reyataz	200-mg capsule	60 capsules	$1,463	$1,756	N/A
Generic	300-mg capsule	30 capsules	$178 to $316	$1,502 to $1,652	$187
Reyataz	300-mg capsule	30 capsules	$1,449	$1,739	N/A

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

ARV Drug (Generic and Brand Names)	Strength, Formulation	Capsules, mLs, Tablets, or Vials	Wholesale Acquisition Cost[b]	Average Wholesale Price[b]	Federal Upper Limit (As of July 31, 2024)[c]
		(Monthly Values, Unless Otherwise Noted)			
Atazanavir/Cobicistat					
Evotaz	300-mg/150-mg tablet	30 tablets	$1,605	$1,927	N/A
Darunavir					
Generic	600-mg tablet	60 tablets	$60 to $1,145	$1,373 to $2,388	Pending
Prezista	600-mg tablet	60 tablets	$2,158	$2,590	N/A
Generic	800-mg tablet	30 tablets	$60 to $1,153	$1,384 to $2,388	Pending
Prezista	800-mg tablet	30 tablets	$2,158	$2,590	N/A
Prezista	100-mg/mL suspension	200 mL	$1,199	$1,439	N/A
Darunavir/Cobicistat					
Prezcobix	800-mg/150-mg tablet	30 tablets	$2,467	$2,960	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	N/A
Tipranavir					
Aptivus	250-mg capsule	120 capsules	$2,054	$2,466	N/A
INSTIs					
Dolutegravir					
Tivicay	50-mg tablet	30 tablets	$2,257	$2,709	N/A
Tivicay	50-mg tablet	60 tablets	$4,514	$5,418	N/A
Raltegravir					
Isentress	400-mg tablet	60 tablets	$1,997	$2,396	N/A

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

ARV Drug (Generic and Brand Names)	Strength, Formulation	Capsules, mLs, Tablets, or Vials	Wholesale Acquisition Cost[b]	Average Wholesale Price[b]	Federal Upper Limit (As of July 31, 2024)[c]
		(Monthly Values, Unless Otherwise Noted)			
Isentress HD	600-mg tablet	60 tablets	$1,997	$2,396	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	$1,659
Selzentry	150-mg tablet	60 tablets	$1,730	$2,076	N/A
Generic	300-mg tablet	60 tablets	$1,141	$1,764	$1,518
Selzentry	300-mg tablet	60 tablets	$1,730	$2,076	N/A
Selzentry	300-mg tablet	120 tablets	$3,460	$4,152	N/A
CD4-Directed Post-Attachment Inhibitor					
Ibalizumab-uiyk					
Trogarzo	200-mg vial	8 vials	$11,840	$14,208	N/A
gp120-Directed Attachment Inhibitor					
Fostemsavir					
Rukobia	600-mg tablet	60 tablets	$9,010	$10,812	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

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

ARV Drug (Generic and Brand Names)	Strength, Formulation	Capsules, mLs, Tablets, or Vials	Wholesale Acquisition Cost[b]	Average Wholesale Price[b]	Federal Upper Limit (As of July 31, 2024)[c]
		(Monthly Values, Unless Otherwise Noted)			
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	$3,981	$4,777	N/A
Darunavir/Cobicistat/Tenofovir Alafenamide/Emtricitabine					
Symtuza	800-mg/150-mg/10-mg/200-mg tablet	30 tablets	$4,717	$5,660	N/A
Dolutegravir/Abacavir/Lamivudine					
Triumeq	50-mg/600-mg/300-mg tablet	30 tablets	$3,748	$4,497	N/A
Dolutegravir/Lamivudine					
Dovato	50-mg/300-mg tablet	30 tablets	$2,977	$3,572	N/A
Dolutegravir/Rilpivirine					
Juluca	50-mg/25-mg tablet	30 tablets	$3,512	$4,215	N/A
Doravirine/Tenofovir Disoproxil Fumarate/Lamivudine					
Delstrigo	100-mg/300-mg/300-mg tablet	30 tablets	$2,680	$3,216	N/A
Efavirenz/Tenofovir Disoproxil Fumarate/Emtricitabine					
Generic	600-mg/300-mg/200-mg tablet	30 tablets	$82 to $252	$302 to $3,414	$54
Atripla	600-mg/300-mg/200-mg tablet	30 tablets	$2,995	$3,594	N/A
Efavirenz/Tenofovir Disoproxil Fumarate/Lamivudine					
Symfi	600-mg/300-mg/150-mg tablet	30 tablets	$1,926	$2,312	N/A

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

ARV Drug (Generic and Brand Names)	Strength, Formulation	Capsules, mLs, Tablets, or Vials	Wholesale Acquisition Cost[b]	Average Wholesale Price[b]	Federal Upper Limit (As of July 31, 2024)[c]
		(Monthly Values, Unless Otherwise Noted)			
Symfi Lo	400-mg/300-mg/150-mg tablet	30 tablets	$1,926	$2,312	N/A
Elvitegravir/Cobicistat/Tenofovir Alafenamide/Emtricitabine					
Genvoya	150-mg/150-mg/10-mg/200-mg tablet	30 tablets	$33,981	$4,777	N/A
Elvitegravir/Cobicistat/Tenofovir Disoproxil Fumarate/Emtricitabine					
Stribild	150-mg/150-mg/300-mg/ 200-mg tablet	30 tablets	$4,176	$5,012	N/A
Rilpivirine/Tenofovir Alafenamide/Emtricitabine					
Odefsey	25-mg/25-mg/200-mg tablet	30 tablets	$3,623	$4,348	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)	$6,624 (every other month)	$7,948 (every other month)	N/A
Cabenuva	400 mg (2 mL) 600 mg (2 mL)	2 vials	$4,416	$5,299	N/A
PK Enhancers (Boosters)					
Cobicistat					
Tybost	150-mg tablet	30 tablets	$297	$357	N/A

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

ARV Drug (Generic and Brand Names)	Strength, Formulation	Capsules, mLs, Tablets, or Vials	Wholesale Acquisition Cost[b]	Average Wholesale Price[b]	Federal Upper Limit (As of July 31, 2024)[c]
		(Monthly Values, Unless Otherwise Noted)			
Ritonavir					
Generic	100-mg tablet	30 tablets	$80 to $160	$278	$74
Norvir	100-mg tablet	30 tablets	$257	$309	N/A

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

[b] Source: Micromedex Red Book [database]. Merative. 2024. Available at: https://www.micromedexsolutions.com.

[c] Source: Federal Upper Limits–March 2024 [database]. Medicare & Medicaid Services. 2024. Available at: https://www.medicaid.gov/medicaid/prescription-drugs/pharmacy-pricing/index.html.

Key: ARV = antiretroviral; CD4 = CD4 T lymphocyte; 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; 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 P450 (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. Some older ARVs—unboosted atazanavir, fosamprenavir, nelfinavir, nevirapine, 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 information regarding drug interactions for these ARVs.

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/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
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

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
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
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
gp120-Directed Attachment Inhibitor							
FTR	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
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; CCR5 = C-C chemokine receptor type 5; 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; gp120 = glycoprotein 120; 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; 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

Updated: September 12, 2024
Reviewed: September 12, 2024

This table provides information on the known or predicted interactions between protease inhibitors (PIs) and non-antiretroviral (ARV) drugs. The term "PI" refers to atazanavir (ATV) or darunavir (DRV) boosted with either ritonavir (RTV or r) or cobicistat (COBI or c). This table does not include interactions for unboosted ATV, fosamprenavir (FPV), lopinavir (LPV), 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 interactions 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 judgment to select the most appropriate alternative medication.

Note: Unboosted ATV, FPV, LPV/r, NFV, and TPV are no longer commonly used in clinical practice in the United States 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. Information regarding these agents may also be found in archived versions of this guideline.

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers			
Antacids	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/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. 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.

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
			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	With Ranitidine • ↔ DRV/r	No dose adjustment needed
Proton Pump Inhibitors	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	↔ PI expected	No dose adjustment needed
	DRV/r	↔ DRV/r Omeprazole AUC ↓ 42%	Consider alternative ARV or acid reducer. If coadministered, monitor for omeprazole effectiveness. 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	ATV/c, ATV/r, DRV/c, DRV/r	↑ alfuzosin expected	Contraindicated
Doxazosin	ATV/c, ATV/r, DRV/c, DRV/r	↑ doxazosin possible	Initiate doxazosin at lowest dose and titrate. Monitor blood pressure. Dose reduction may be necessary.
Tamsulosin	ATV/c, ATV/r, DRV/c, DRV/r	↑ tamsulosin expected	Do not coadminister unless benefits outweigh risks. If coadministered, monitor blood pressure.

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
Terazosin	ATV/c, ATV/r, DRV/c, DRV/r	↔ or ↑ terazosin possible	Initiate terazosin at lowest dose and titrate. Monitor blood pressure. Dose reduction may be necessary.
Silodosin	ATV/c, ATV/r, DRV/c, DRV/r	↑ silodosin expected	Contraindicated
Antibacterials—Antimycobacterials			
Bedaquiline	ATV/c, ATV/r, DRV/c, DRV/r	• ↑ bedaquiline possible	Do not coadminister unless benefits outweigh risks. If coadministered, consider therapeutic drug monitoring and monitor for bedaquiline-related adverse effects, including hepatotoxicity and QTc prolongation.
Rifabutin	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%	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.
	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%	
	ATV/c, DRV/c	↑ rifabutin expected ↓ COBI expected	Do not coadminister.
Rifampin	ATV/c, ATV/r, DRV/c, DRV/r	↓ 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.

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
Rifapentine	ATV/c, ATV/r, DRV/c, DRV/r	Daily and Weekly Dosing • ↓ PI expected	Do not coadminister.
Antibacterials—Macrolides			
Azithromycin	ATV/c, ATV/r	↑ azithromycin possible	No dose adjustment needed
	DRV/c, DRV/r	↔ azithromycin expected	No dose adjustment needed
Clarithromycin	ATV/c, ATV/r, DRV/c	↑ clarithromycin expected ↑ ATV/r and PI/c expected	Consider alternative ARV or azithromycin.
	DRV/r	DRV/r ↑ clarithromycin AUC 57% 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	ATV/c, ATV/r, DRV/c, DRV/r	↑ erythromycin expected ↑ PI expected	Consider alternative ARV or use azithromycin.
Anticoagulants			
Apixaban	ATV/c, ATV/r, DRV/c, DRV/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%.

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
Dabigatran	ATV/c, ATV/r	With COBI 150 mg Alone • Dabigatran AUC ↑ 110% to 127% With ATV/r • ↑ dabigatran expected	Reduction of Risk of Stroke and Systemic Embolism in Nonvalvular Atrial Fibrillation in Adult Patients • CrCl >30 mL/min: no dose adjustment needed • CrCl ≤30 mL/min: do not coadminister. Treatment and Reduction in the Risk of Recurrence of DVT and PE or Prophylaxis of DVT and PE Following Hip Replacement Surgery in Adult Patients • CrCl ≥50 mL/min: no dose adjustment needed • CrCl <50 mL/min: do not coadminister.
	DRV/c, DRV/r	With DRV/c • Single dose DRV/c: dabigatran AUC ↑ 164% • After 14 days of DRV/c: dabigatran AUC ↑ 88% With DRV/r • Single dose DRV/r: dabigatran AUC ↑ 72% • After 14 days of daily DRV/r: dabigatran AUC ↑ 18%	
Edoxaban	ATV/c, ATV/r, DRV/c	↑ edoxaban expected	Treatment of Nonvalvular Atrial Fibrillation • No dose adjustment needed Treatment of DVT and PE • Reduce edoxaban dose to 30 mg once daily.
	DRV/r	↑ edoxaban expected	Treatment of Nonvalvular Atrial Fibrillation • No dose adjustment needed Treatment of DVT and PE • No dose adjustment needed
Rivaroxaban	ATV/c, ATV/r, DRV/c, DRV/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	ATV/c, DRV/c	↑ warfarin possible	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.
	ATV/r, DRV/r	↓ warfarin possible	
Antidepressants, Anxiolytics, and Antipsychotics Also see the Sedative/Hypnotics section below			
Antidepressants, Anxiolytics			
Bupropion	ATV/r, DRV/r	↓ bupropion possible	Titrate bupropion dose based on clinical response.
	ATV/c, DRV/c	↔ bupropion expected	No dose adjustment needed
Buspirone	ATV/c, ATV/r, DRV/c, DRV/r	↑ 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.
Desvenlafaxine	ATV/c, ATV/r, DRV/c, DRV/r	↑ desvenlafaxine possible	No dose adjustment needed
Duloxetine	ATV/c, DRV/c	↑ duloxetine possible	No dose adjustment needed
	ATV/r, DRV/r	↑ or ↓ duloxetine possible	
Mirtazapine	ATV/c, ATV/r, DRV/c, DRV/r	↑ mirtazapine possible	Monitor for mirtazapine-related adverse events. Mirtazapine dose reduction may be necessary.
Nefazodone	ATV/c, ATV/r, DRV/c, DRV/r	↑ nefazodone expected ↑ PI possible	Monitor for nefazodone-related adverse events and 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
Selective Serotonin Reuptake Inhibitors (e.g., citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, vortioxetine)	DRV/r	Paroxetine AUC ↓ 39% Sertraline AUC ↓ 49%	Titrate SSRI dose based on clinical response.
	ATV/c, ATV/r, DRV/c	↑ or ↓ SSRI possible	Titrate SSRI dose using the lowest available initial or maintenance dose.
Trazodone	ATV/c, ATV/r, DRV/c, DRV/r	RTV 200 mg Twice Daily (For 2 Days) • Trazodone ↑ AUC 240%	Administer lowest dose of trazodone and titrate dose based on clinical response. Monitor for trazodone-related adverse events, including CNS and CV adverse events.
Tricyclic Antidepressants (e.g., amitriptyline, doxepin, nortriptyline)	ATV/c, ATV/r, DRV/c, DRV/r	↑ TCA expected	Administer lowest possible TCA dose and titrate based on clinical assessment and/or drug concentrations. Monitor for TCA-related adverse events.
Venlafaxine	ATV/c, ATV/r, DRV/c, DRV/r	↑ venlafaxine and O-desmethylvenlafaxine expected	Monitor for venlafaxine-related adverse events. Consider venlafaxine dose reduction.
Antipsychotics			
Aripiprazole	ATV/c, ATV/r, DRV/c, DRV/r	↑ aripiprazole expected	Administer 25% of the usual aripiprazole dose. Titrate dose based on clinical monitoring for effectiveness/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/c, ATV/r, DRV/c, DRV/r	↑ brexpiprazole expected	Administer 25% of the usual brexpiprazole dose. Titrate the dose based on clinical monitoring for effectiveness/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.

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
Cariprazine	ATV/c, ATV/r, DRV/c, DRV/r	↑ 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 • 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	ATV/c, ATV/r, DRV/c, DRV/r	↑ iloperidone expected	Decrease iloperidone dose by 50%.
Lumateperone	ATV/c, ATV/r, DRV/c, DRV/r	↑ lumateperone expected	Do not coadminister.
Lurasidone	ATV/c, ATV/r, DRV/c, DRV/r	↑ lurasidone expected	Contraindicated
Olanzapine, Olanzapine/Samidorphan	ATV/c, DRV/c	↔ olanzapine expected ↑ samidorphan possible	No dose adjustment needed
	ATV/r, DRV/r	↓ olanzapine possible	Monitor for therapeutic effectiveness of olanzapine.
Other Antipsychotics CYP3A4 and/or CYP2D6 substrates (e.g., clozapine, perphenazine, risperidone, thioridazine)	ATV/c, ATV/r, DRV/c, DRV/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.

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
Pimavanserin	ATV/c, ATV/r, DRV/c, DRV/r	↑ pimavanserin expected	Reduce pimavanserin dose to 10 mg once daily.
Pimozide	ATV/c, ATV/r, DRV/c, DRV/r	↑ pimozide expected	Contraindicated
Quetiapine	ATV/c, ATV/r, DRV/c, DRV/r	↑ 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	ATV/c, ATV/r, DRV/c, DRV/r	↑ ziprasidone expected	Monitor for ziprasidone-related adverse events, including QTc prolongation.
Antimigraine			
Ergot Derivatives	ATV/c, ATV/r, DRV/c, DRV/r	↑ dihydroergotamine, ergotamine, and methylergonovine expected	Contraindicated
Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonists			
Atogepant	ATV/c, ATV/r, DRV/c, DRV/r	↑ atogepant expected	Chronic migraine: Do not coadminister. Episodic migraine: Administer atogepant at a dose of 10 mg once daily.
Rimegepant	ATV/c, ATV/r, DRV/c, DRV/r	↑ rimegepant expected	Do not coadminister.
Ubrogepant	ATV/c, ATV/r, DRV/c, DRV/r	↑ ubrogepant 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
Zavegepant	ATV/r, ATV/c, DRV/c	↑ zavegepant expected	Do not coadminister.
	DRV/r	↔ zavegepant expected	No dose adjustment needed
Serotonin 5-HT1B, 1D Receptor Agonists			
Almotriptan	ATV/c, ATV/r, DRV/c, DRV/r	↑ almotriptan expected	Administer single dose of almotriptan 6.25 mg. Maximum dose should not exceed 12.5 mg in a 24-hour period.
Eletriptan	ATV/c, ATV/r, DRV/c, DRV/r	↑ eletriptan expected	Contraindicated
Frovatriptan, Naratriptan, Rizatriptan, Sumatriptan Zolmitriptan	ATV/c, ATV/r, DRV/c, DRV/r	↔ triptan expected	No dose adjustment needed
Antifungals			
Fluconazole	ATV/c, ATV/r, DRV/c, DRV/r	↔ PI expected ↔ fluconazole expected	No dose adjustment needed
Isavuconazole	ATV/c, DRV/c	↑ isavuconazole expected ↓ PI possible	Contraindicated
	ATV/r, DRV/r	↑ isavuconazole expected ↓ PI possible	If coadministered, monitor isavuconazole concentrations and monitor for isavuconazole-related adverse events. Monitor for PI tolerability.
Ibrexafungerp	ATV/c, ATV/r, DRV/c, DRV/r	↑ ibrexafungerp expected	Reduce ibrexafungerp dose to 150 mg twice daily.
Itraconazole	ATV/c, ATV/r, DRV/c, DRV/r	↑ itraconazole expected ↑ PI expected	Itraconazole doses >200 mg/day are not recommended unless dosing is guided by itraconazole concentrations.

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
Posaconazole	ATV/r	ATV AUC ↑ 146% ↔ posaconazole possible	If coadministered, monitor for PI-related adverse events.
	ATV/c, DRV/c, DRV/r	↑ PI expected ↔ posaconazole possible	
Voriconazole	ATV/c, DRV/c	No data	**Do not coadminister** voriconazole and RTV or COBI unless benefits outweigh risks. If coadministered, monitor voriconazole concentration and adjust dose accordingly.
	ATV/r, DRV/r	RTV 100 mg twice daily ↓ voriconazole AUC 39%	
Antimalarials			
Artemether/Lumefantrine	ATV/c, DRV/c	↑ lumefantrine expected ↑ artemether possible	Clinical significance is unknown. If coadministered, monitor closely for antimalarial effectiveness and lumefantrine-related adverse events, including QTc prolongation.
	DRV/r	↔ artemether expected ↔ DHA[a] expected Lumefantrine AUC ↑ 175% ↔ DRV	
Artesunate	ATV/c	↑ DHA[a] possible	Monitor for artesunate-related adverse effects.
	DRV/c	↔ DHA[a] expected	No dose adjustment needed
	ATV/r, DRV/r	↓ DHA[a] possible	Monitor for clinical response to artesunate.

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
Atovaquone/Proguanil	ATV/r, DRV/r	With ATV/r • Atovaquone AUC ↓ 46% • Proguanil AUC ↓ 41% With DRV/r • ↓ atovaquone/proguanil possible	Clinical significance is unknown. Consider alternative ARV or malaria prophylaxis.
	ATV/c, DRV/c	↔ atovaquone/proguanil expected	No dose adjustment needed
Mefloquine	ATV/c, ATV/r, DRV/c, DRV/r	With RTV 200 mg Twice Daily • RTV AUC ↓ 31% and C_{min} ↓ 43% • ↔ mefloquine With ATV (Unboosted), PI/c, or PI/r • ↑ 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	ATV/c, ATV/r, DRV/c, DRV/r	Clopidogrel active metabolite AUC ↓ 69% in people with HIV on RTV or COBI-boosted regimens compared with healthy volunteers without HIV. Impaired platelet inhibition observed in people with HIV.	Do not coadminister.
Prasugrel	ATV/c, ATV/r, DRV/c, DRV/r	Prasugrel active metabolite AUC ↓ 52% in people with HIV on RTV or COBI-boosted regimens compared to healthy volunteers without HIV. Adequate platelet inhibition observed in people with HIV.	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
Ticagrelor	ATV/c, ATV/r, DRV/c, DRV/r	↑ ticagrelor expected	Do not coadminister.
Vorapaxar	ATV/c, ATV/r, DRV/c, DRV/r	↑ vorapaxar expected	Do not coadminister.
Antipneumocystis and Antitoxoplasmosis			
Atovaquone Oral suspension	ATV/r	↔ atovaquone	No dose adjustment needed
	ATV/c, DRV/c, DRV/r	↔ atovaquone expected	No dose adjustment needed
Antiseizure			
Carbamazepine	ATV/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.
	DRV/r	Carbamazepine AUC ↑ 45% ↔ DRV	Monitor anticonvulsant concentration and adjust dose accordingly.
	ATV/c, DRV/c	↑ carbamazepine possible ↓ COBI expected ↓ PI expected	Contraindicated
Eslicarbazepine	ATV/c, ATV/r, DRV/c, DRV/r	↓ PI possible	Consider alternative ARV or anticonvulsant. If coadministration is necessary, monitor for virologic response. Consider monitoring anticonvulsant and PI concentrations.
Ethosuximide	ATV/c, ATV/r, DRV/c, DRV/r	↑ ethosuximide possible	Monitor for ethosuximide-related adverse events.
Lamotrigine	ATV/r	Lamotrigine AUC ↓ 32%	A dose increase of lamotrigine may be needed; monitor

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	lamotrigine concentration or consider alternative ARV or anticonvulsant.
	ATV/c	No data	Monitor anticonvulsant concentration and adjust dose accordingly.
	DRV/c	↔ lamotrigine expected	No dose adjustment needed.
Oxcarbazepine	ATV/c, ATV/r, DRV/c, DRV/r	↓ PI possible	Consider alternative ARV or anticonvulsant. If coadministration is necessary, monitor for virologic response. Consider monitoring anticonvulsant and PI concentrations.
Phenobarbital	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.
	ATV/c, DRV/c	↓ COBI expected ↓ PI expected	Contraindicated
Phenytoin	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.
	ATV/c, DRV/c	↓ COBI expected ↓ PI expected	Contraindicated
Primidone	ATV/c, ATV/r, DRV/c, DRV/r	↓ PI expected	Do not coadminister.
Valproic Acid	ATV/c, ATV/r, DRV/c, DRV/r	↓ 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
Antivirals—Hepatitis C			
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	
	ATV/c, DRV/c	↑ grazoprevir expected	
Glecaprevir/Pibrentasvir	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 ↑ fivefold • ↔ pibrentasvir	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/c, DRV/c, DRV/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/c, DRV/c	↔ sofosbuvir and velpatasvir expected	No dose adjustment needed
Sofosbuvir/Velpatasvir/ Voxilaprevir	ATV/c, ATV/r	With ATV/r • Voxilaprevir AUC ↑ 4.3-fold • Velpatasvir AUC ↑ 93% • Sofosbuvir AUC ↑ 40%	Do not coadminister.
	DRV/c, DRV/r	With DRV/r • Voxilaprevir AUC ↑ 2.4-fold • ↔ DRV/r, velpatasvir, and sofosbuvir	No dose adjustment needed

Table 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
Antivirals—Miscellaneous (e.g., for CMV, Mpox)			
Brincidofovir	ATV/c, ATV/r, DRV/c, DRV/r	↑ 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).
Cidofovir	ATV/c, ATV/r, DRV/c, DRV/r	↔ cidofovir	No dose adjustment needed
Tecovirimat	ATV/c, ATV/r, DRV/c, DRV/r	↔ tecovirimat	No dose adjustment needed
Antivirals—SARS-CoV-2			
Molnupiravir	ATV/c, ATV/r, DRV/c, DRV/r	↔ molnupiravir	No dose adjustment needed
Remdesivir	ATV/c, ATV/r, DRV/c, DRV/r	↔ remdesivir	No dose adjustment needed
Ritonavir-Boosted Nirmatrelvir	ATV/r, ATV/c, DRV/c, DRV/r	↑ PI expected ↑ ritonavir-boosted nirmatrelvir expected	No dose adjustment needed. Monitor for increased ritonavir-boosted nirmatrelvir and PI-related adverse events.
Beta-Agonists, Long-Acting Inhaled			
Arformoterol, Formoterol	ATV/c, ATV/r	↑ arformoterol possible	No dose adjustment needed
	DRV/c, DRV/r	↔ arformoterol expected	No dose adjustment needed
Indacaterol	ATV/c, ATV/r, DRV/c, DRV/r	With RTV 300 mg Twice Daily • Indacaterol AUC ↑ 1.7-fold	No dose adjustment needed in patients receiving indacaterol 75 mcg daily.
Olodaterol	ATV/c, ATV/r, DRV/c, DRV/r	↑ olodaterol expected	No dose adjustment needed
Salmeterol	ATV/c, ATV/r, DRV/c, DRV/r	↑ salmeterol possible	Do not coadminister, due to potential increased risk of salmeterol-related CV 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
Cardiac Medications			
Antiarrhythmics			
Amiodarone	ATV/r	↑ amiodarone possible ↑ PI possible	Contraindicated
	ATV/c, DRV/c, DRV/r	↑ 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.
Digoxin	ATV/c, ATV/r, DRV/c, DRV/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.
Disopyramide	ATV/c, ATV/r, DRV/c, DRV/r	↑ disopyramide possible	Do not coadminister.
Dofetilide	ATV/c, ATV/r, DRV/c, DRV/r	↑ dofetilide possible	Do not coadminister.
Dronedarone	ATV/c, ATV/r, DRV/c, DRV/r	↑ dronedarone expected	Contraindicated
Flecainide	ATV/c, ATV/r, DRV/c, DRV/r	↑ flecainide possible	Consider alternative ARV or antiarrhythmic. If coadministered, monitor flecainide concentrations and for antiarrhythmic-related adverse events.
Lidocaine	ATV/c, ATV/r, DRV/c, DRV/r	↑ lidocaine possible	Consider alternative ARV or antiarrhythmic. If coadministered, monitor lidocaine concentrations and for antiarrhythmic-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
Mexiletine	ATV/c, ATV/r, DRV/c, DRV/r	↑ mexiletine possible	Consider alternative ARV or antiarrhythmic. If coadministered, monitor mexiletine concentrations and for antiarrhythmic-related adverse events.
Propafenone	ATV/c, ATV/r, DRV/c, DRV/r	↑ propafenone possible	Do not coadminister.
Quinidine	ATV/r	↑ quinidine expected	Contraindicated
	ATV/c, DRV/c, DRV/r	↑ quinidine possible	Do not coadminister.
Sotalol	ATV/c, ATV/r, DRV/c, DRV/r	↔ sotalol expected	No dose adjustment needed
Beta-Blockers			
Atenolol, Labetalol	ATV/c, ATV/r, DRV/c, DRV/r	↑ beta-blockers possible	No dose adjustment needed
Bisoprolol, Carvedilol, Metoprolol, Nebivolol	ATV/c, ATV/r, DRV/c, DRV/r	↑ 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).
Calcium Channel Blockers			
Amlodipine, Diltiazem, Felodipine, Nifedipine, Verapamil	ATV/c, ATV/r, DRV/c, DRV/r	↑ dihydropyridine possible ↑ verapamil possible	Titrate CCB dose and monitor closely. ECG monitoring is recommended when CCB is used with ATV.
Diltiazem	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	↑ diltiazem possible	Titrate diltiazem dose according to clinical response and 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
Cardiac—Other			
Bosentan	ATV/c, ATV/r, DRV/c, DRV/r	With ATV (Unboosted) • ↓ ATV expected With PI/r or PI/c • ↑ bosentan 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.
Eplerenone	ATV/c, ATV/r, DRV/c, DRV/r	↑ eplerenone expected	Contraindicated
Ivabradine	ATV/c, ATV/r, DRV/c, DRV/r	↑ ivabradine expected	Contraindicated
Mavacamten	ATV/c, ATV/r, DRV/c, DRV/r	↑ mavacamten expected	Contraindicated
Ranolazine	ATV/c, ATV/r, DRV/c, DRV/r	↑ ranolazine 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
	ATV/c, ATV/r, DRV/c	↔ 17-BMP 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
Budesonide, Ciclesonide, Fluticasone, Mometasone Inhaled or intranasal	ATV/c, ATV/r, DRV/c, DRV/r	↑ 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).
Betamethasone, Budesonide Systemic	ATV/c, ATV/r, DRV/c, DRV/r	↑ 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	ATV/c, ATV/r, DRV/c, DRV/r	↑ glucocorticoids possible ↓ PI possible	Consider alternative corticosteroid for long-term use. If coadministration is necessary, monitor virologic response to ART.
Prednisone, Prednisolone Systemic	ATV/c, ATV/r, DRV/c, DRV/r	↑ prednisolone possible	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.
Betamethasone, Methylprednisolone, Triamcinolone Local injections, including intra-articular, epidural, or intra-orbital	ATV/c, ATV/r, DRV/c, DRV/r	↑ glucocorticoids expected	Do not coadminister. Coadministration can result in adrenal insufficiency and Cushing's syndrome.

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
Glucose-Lowering			
Canagliflozin	ATV/c, DRV/c	↔ canagliflozin	No dose adjustment needed
	ATV/r, DRV/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 W**ith eGFR ≥60 mL/min/1.73 m²** • Canagliflozin dose may be increased to 300 mg daily. In Patients With eGFR <60 mL/min/1.73 m² • Consider adding another antihyperglycemic agent.
Saxagliptin	ATV/c, ATV/r, DRV/c, DRV/r	↑ saxagliptin expected	Limit saxagliptin dose to 2.5 mg once daily.
Dapagliflozin/Saxagliptin	ATV/c, ATV/r, DRV/c, DRV/r	↑ 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.
Herbal Products			
St. John's Wort	ATV/c, ATV/r, DRV/c, DRV/r	↓ PI expected	Contraindicated
Hormonal Therapies—Contraceptives			
Injectable Contraceptives Depot MPA	ATV/c, ATV/r, DRV/c, DRV/r	↔ 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
Oral Contraceptives (e.g., desogestrel, drospirenone, ethinyl estradiol, levonorgestrel, norgestimate, norethindrone)	ATV/c	Drospirenone AUC ↑ 130% Ethinyl estradiol AUC ↓ 22%	Contraindicated with drospirenone-containing hormonal contraceptive due to potential for hyperkalemia. Use alternative ARV or alternative 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]
		↑ drospirenone expected ↔ estetrol	Clinical monitoring is recommended due to the potential for hyperkalemia. Use alternative ARV or contraceptive methods.
	DRV/c	Drospirenone AUC ↑ 58% Ethinyl estradiol AUC ↓ 30%	Clinical monitoring is recommended due to the potential for hyperkalemia. Use alternative ARV or contraceptive methods.
	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.
Subdermal Implant Contraceptives (e.g., etonogestrel, levonorgestrel)	ATV/c, ATV/r, DRV/c, DRV/r	↑ etonogestrel, levonorgestrel 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
Transdermal Contraceptives (e.g., ethinyl estradiol/norelgestromin, ethinyl estradiol/levonorgestrel)	ATV/c, ATV/r, DRV/c, DRV/r	↓ ethinyl estradiol possible with ritonavir ↑ ethinyl estradiol possible with cobicistat ↑ norelgestromin, levonorgestrel possible	No dose adjustment needed
Vaginal Ring Contraceptives (e.g., etonogestrel/ethinyl estradiol, segesterone/ethinyl estradiol)	ATV/r	Ethinyl estradiol AUC ↓ 26% Etonogestrel AUC ↑ 79%	No dose adjustment needed with etonogestrel/ethinyl estradiol vaginal rings. Use alternative ARV or contraceptive methods with segesterone/ethinyl estradiol vaginal rings.
	ATV/c, DRV/c, DRV/r	↓ ethinyl estradiol possible with ritonavir ↑ ethinyl estradiol possible with cobicistat	
Emergency Contraceptives Levonorgestrel (oral)	ATV/c, ATV/r, DRV/c, DRV/r	↑ levonorgestrel expected	No dose adjustment needed
Hormonal Therapies—Gender Affirming and Menopause			
Estradiol	ATV/c, DRV/c	↓ or ↑ estradiol possible	Adjust estradiol dose as needed based on clinical effects and endogenous hormone concentrations.
	ATV/r, DRV/r	↓ estradiol possible	
5-Alpha Reductase Inhibitors (e.g., dutasteride, finasteride)	ATV/c, ATV/r, DRV/c, DRV/r	↑ dutasteride possible ↑ finasteride possible	Adjust dutasteride dose as needed based on clinical effects and endogenous hormone concentrations. No dose adjustment needed for finasteride.
Testosterone	ATV/c, ATV/r, DRV/c, DRV/r	↑ testosterone possible	Adjust testosterone dose as needed based on clinical effects and endogenous hormone concentrations.
Other Gender-Affirming Medications	ATV/c, ATV/r, DRV/c, DRV/r	↔ goserelin, leuprolide acetate, and spironolactone 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
Menopausal Hormone Replacement Therapy (e.g., conjugated estrogens, drospirenone, estradiol, MPA, progesterone)	ATV/c, ATV/r, DRV/c, DRV/r	↓ or ↑ estrogen possible with estradiol or conjugated estrogen (equine and synthetic)	Adjust estrogen dose as needed based on clinical effects.
	ATV/c, ATV/r, DRV/c, DRV/r	↑ drospirenone possible ↑ MPA ↑ micronized progesterone See the Hormonal Therapies—Contraceptives section for other progestin-PI interactions.	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.
Immunosuppressants			
Cyclosporine, Sirolimus, Tacrolimus	ATV/c, ATV/r, DRV/c, DRV/r	↑ 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.
	ATV/c, ATV/r	↑ 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.

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
Lipid-Modifying			
Atorvastatin	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.
Fluvastatin	ATV/c, DRV/c	↑ fluvastatin expected	Administer the lowest effective fluvastatin dose while monitoring for adverse events.
	ATV/r, DRV/r	↑ or ↓ fluvastatin possible	
Lomitapide	ATV/c, ATV/r, DRV/c, DRV/r	↑ lomitapide expected	Contraindicated
Lovastatin	ATV/c, ATV/r, DRV/c, DRV/r	Significant ↑ lovastatin expected	Contraindicated
Pitavastatin	ATV/c, DRV/c	No data	No dose adjustment needed. Monitor for pitavastatin-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
	ATV/r, DRV/r	With ATV/r • ↔ pitavastatin expected • ↔ ATV/r expected With DRV/r • ↓ pitavastatin AUC 26% • ↔ DRV/r	No dose adjustment needed
Pravastatin	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.
Rosuvastatin	ATV/r	Rosuvastatin AUC ↑ 3-fold and C_{max} ↑ 7-fold	Administer the lowest effective rosuvastatin dose while monitoring for adverse events. Do not exceed rosuvastatin 10 mg daily.
	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.
	DRV/r	Rosuvastatin AUC ↑ 48% and C_{max} ↑ 2.4-fold	Administer the lowest effective rosuvastatin dose while monitoring for adverse events.
Simvastatin	ATV/c, ATV/r, DRV/c, DRV/r	Significant ↑ simvastatin 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
Narcotics and Treatment for Opioid Dependence			
Buprenorphine Sublingual, buccal, or implant	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.
	ATV/c, DRV/c	↑ buprenorphine possible	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	ATV/c, ATV/r, DRV/c, DRV/r	↑ fentanyl possible	Monitor for fentanyl-related adverse events, including potentially fatal respiratory depression.
Lofexidine	ATV/c, ATV/r, DRV/c, DRV/r	↑ lofexidine possible	Monitor for lofexidine-related adverse events, including symptoms of orthostasis and bradycardia.
Methadone	ATV/c, DRV/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.
	ATV/r, DRV/r	ATV/r and DRV/r ↓ R-methadone[d] AUC 16% to 18%	Opioid withdrawal is unlikely but may occur. Monitor for opioid withdrawal and increase methadone dose as clinically indicated.
Oxycodone	ATV/c, ATV/r, DRV/c, DRV/r	↑ oxycodone expected	Monitor for opioid-related adverse events, including potentially fatal respiratory depression. Oxycodone 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
Tramadol	ATV/c, ATV/r, DRV/c, DRV/r	↑ 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/c, ATV/r, DRV/c, DRV/r	RTV 600 mg twice daily (for 5 days) ↑ avanafil AUC 13-fold and ↑ C_{max} 2.4-fold	Do not coadminister.
Sildenafil	ATV/c, ATV/r, DRV/c, DRV/r	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 sildenafil-related adverse events. Contraindicated for treatment of PAH.
Tadalafil	ATV/c, ATV/r, DRV/c, DRV/r	RTV 200 mg twice daily ↑ tadalafil AUC 124%	For Treatment of Erectile Dysfunction *As-Needed Use* • Start with tadalafil 5 mg and do not exceed a single dose of tadalafil 10 mg every 72 hours. Monitor for tadalafil-related adverse events. *Once-Daily Use* • Do not exceed tadalafil 2.5 mg once daily. Monitor for tadalafil-related adverse events. 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.

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
			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. Monitor for tadalafil-related adverse events.
Vardenafil	ATV/c, ATV/r, DRV/c, DRV/r	RTV 600 mg twice daily ↑ vardenafil AUC 49-fold	Start with vardenafil 2.5 mg every 72 hours and monitor for vardenafil-related adverse events.
Sedative/Hypnotics			
Benzodiazepines			
Alprazolam, Clonazepam, Diazepam	ATV/c, ATV/r, DRV/c, DRV/r	↑ 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	ATV/c, ATV/r, DRV/c, DRV/r	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	ATV/c, ATV/r, DRV/c, DRV/r	↑ 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.
Triazolam	ATV/c, ATV/r, DRV/c, DRV/r	↑ triazolam expected RTV 200 mg twice daily ↑ triazolam half-life 1,200% and ↑ AUC 2,000%	Contraindicated
Orexin Receptor Antagonist			
Daridorexant, Lemborexant, Suvorexant	ATV/c, ATV/r, DRV/c, DRV/r	↑ daridorexant, lemborexant, suvorexant expected	Do not coadminister.
Other Sedatives			
Eszopiclone	ATV/c, ATV/r, DRV/c, DRV/r	↑ eszopiclone expected	Start with lowest dose and increase to a maximum of 2 mg daily; monitor for eszopiclone-related adverse events.
Zolpidem	ATV/c, ATV/r, DRV/c, DRV/r	↑ zolpidem possible	Initiate zolpidem at a low dose and monitor for zolpidem-related adverse events. Dose reduction may be necessary.
Miscellaneous			
Calcifediol	ATV/c, ATV/r, DRV/c, DRV/r	↑ 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	ATV/c, ATV/r, DRV/c, DRV/r	↑ cisapride 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
Colchicine	ATV/c, ATV/r, DRV/c, DRV/r	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)
Dronabinol	ATV/c, ATV/r, DRV/c, DRV/r	↑ dronabinol possible	Monitor for dronabinol-related adverse events.
Eluxadoline	ATV/c, ATV/r, DRV/c, DRV/r	↑ eluxadoline expected	Administer eluxadoline at a dose of 75 mg twice daily and monitor for eluxadoline-related adverse events.
Finerenone	ATV/c, ATV/r, DRV/c, DRV/r	↑ finerenone expected	Contraindicated
Flibanserin	ATV/c, ATV/r, DRV/c, DRV/r	↑ flibanserin expected	Contraindicated
Naloxegol	ATV/c, ATV/r, DRV/c, DRV/r	↑ naloxegol expected	Contraindicated
Praziquantel	ATV/c, ATV/r, DRV/c, DRV/r	↑ praziquantel possible	Consider alternative ARV. If coadministration is necessary, monitor for praziquantel-related adverse events.

[a] DHA is an active metabolite of artemether and artesunate.

[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.

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

[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
↔ = less than 20% change in AUC

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; CMV = cytomegalovirus; CV = cardiovascular; CYP = cytochrome P; DHA = dihydroartemisinin; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DVT = deep vein thrombosis; 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; PE = pulmonary embolism; 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

Updated: September 12, 2024
Reviewed: September 12, 2024

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

Oral doses of RPV at 75 mg and 300 mg once daily (equivalent to 3 and 12 times the recommended dose) were associated with prolonged QTc (or QT corrected for heart rate) 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.

Nevirapine (NVP) is no longer commonly used in clinical practice in the United States and is not included in this table. Please refer to the U.S. Food and Drug Administration product labels for information regarding drug interactions between NVP and concomitant medications. Information may also be found in archived versions of this guideline.

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers			
Antacids	DOR, EFV	↔ 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.

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
H2 Receptor Antagonists	DOR	↔ DOR 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 and C_{min}	No dose adjustment needed
	EFV	↔ EFV expected	
	ETR	With Omeprazole 40 mg Daily • ETR AUC ↑ 41%	
	RPV IM	↔ RPV expected	No dose adjustment needed
	RPV PO	With Omeprazole 20 mg Daily • RPV AUC ↓ 40% to 65% 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	↓ 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	↓ 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.

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
Antibacterials—Antimycobacterials			
Bedaquiline	DOR, RPV IM, RPV PO	↔ bedaquiline expected	No dose adjustment needed
	EFV, ETR	↓ bedaquiline possible	Do not coadminister.
Rifabutin	DOR	DOR AUC ↓ 50%	Increase DOR dose to 100 mg twice daily. No dose adjustment is needed for rifabutin.
	EFV	Rifabutin ↓ 38%	Increase rifabutin dose to 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.
	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 during coadministration. No dose adjustment for rifabutin is needed.
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.
	RPV IM	↓ RPV possible	Contraindicated
	RPV PO	RPV AUC ↓ 80%	Contraindicated
Rifapentine	DOR	Once-Weekly Rifapentine Plus Isoniazid and DOR 100 mg Twice Daily 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	Daily Rifapentine (Max 600 mg) With EFV • ↔ EFV	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
		Weekly Rifapentine (Max 900 mg) With EFV • ↔ EFV	
	ETR	↓ ETR possible	Do not coadminister.
	RPV IM, RPV PO	↓ RPV possible	Contraindicated
Antibacterials—Macrolides			
Azithromycin	DOR, EFV, ETR, RPV IM, RPV PO	↔ 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.
	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.
	EFV, ETR	↑ EFV and ETR 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

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	↓ apixaban possible	Consider alternative ARV or anticoagulant therapy.
Dabigatran, Edoxaban	DOR, EFV, ETR, RPV IM, RPV PO	↔ DOAC expected	No dose adjustment needed
Rivaroxaban	DOR, RPV IM, RPV PO	↔ rivaroxaban expected	No dose adjustment needed
	EFV, ETR	↓ rivaroxaban possible	Consider alternative ARV or anticoagulant therapy.
Warfarin	DOR, RPV IM, RPV PO	↔ warfarin expected	No dose adjustment needed
	EFV, ETR	↑ or ↓ warfarin possible	Monitor INR and adjust warfarin dose accordingly.
Antiseizure			
Carbamazepine, Phenobarbital, Phenytoin, Primidone	DOR	↓ DOR possible	Contraindicated. After stopping antiseizure medication, wait 4 weeks before initiating DOR.
	EFV	Carbamazepine Plus EFV • Carbamazepine AUC ↓ 27% • EFV AUC ↓ 36% Phenytoin Plus EFV • ↓ EFV • ↑ or ↓ phenytoin possible Phenobarbital or Primidone Plus EFV • ↓ EFV and antiseizure agent possible	Consider alternative ARV or antiseizure medication. If coadministration is necessary, monitor antiseizure drug and EFV concentrations.
	ETR	↓ antiseizure agent and ETR possible	Do not coadminister.
	RPV IM, RPV PO	↓ RPV possible	Contraindicated
Eslicarbazepine	DOR, EFV, ETR, RPV IM, RPV PO	↓ NNRTI possible	Consider alternative ARV or antiseizure medication. If coadministration is necessary, monitor virologic response and consider monitoring plasma concentrations of ARVs.

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
Oxcarbazepine	DOR, RPV IM, RPV PO	↓ NNRTI possible	Contraindicated
	EFV, ETR	↓ NNRTI possible	Consider alternative ARV or antiseizure medication. If coadministration is necessary, monitor virologic response and consider monitoring plasma concentrations of ARVs.
Ethosuximide, Lacosamide, Tiagabine, Zonisamide	DOR, RPV IM, RPV PO	↔ antiseizure agent expected	No dose adjustment needed
	EFV, ETR	↓ antiseizure agent possible	Monitor seizure control. Consider anticonvulsant therapeutic drug monitoring.
Lamotrigine	DOR, ETR, 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.			
Antidepressants and Anxiolytics			
Bupropion	DOR, ETR, RPV IM, RPV PO	↔ bupropion expected	No dose adjustment needed
	EFV	Bupropion AUC ↓ 55%	Titrate bupropion dose based on clinical response.
Citalopram, Escitalopram	DOR, RPV IM, RPV PO	↔ antidepressant expected	No dose adjustment needed
	EFV, ETR	↓ antidepressant possible	Titrate antidepressant dose based on clinical response.
Desvenlafaxine, Venlafaxine	DOR, EFV, ETR, RPV IM, RPV PO	↔ antidepressant expected	No dose adjustment needed
Duloxetine	DOR, EFV, ETR, RPV IM, RPV PO	↔ antidepressant expected	No dose adjustment needed
Fluoxetine, Fluvoxamine	DOR, EFV, ETR, RPV IM, RPV PO	↔ antidepressant expected	No dose adjustment needed
Mirtazapine	DOR, RPV IM, RPV PO	↔ mirtazapine 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	↓ mirtazapine possible	Monitor antidepressant effect. Titrate dose as necessary based on clinical response.
Nefazodone	DOR, RPV IM, RPV PO	↑ NNRTI possible	No dose adjustment needed
	EFV, ETR	↓ nefazodone expected ↑ NNRTI possible	Monitor antidepressant effect. Titrate dose as necessary based on clinical response.
Paroxetine	DOR, ETR, RPV IM, RPV PO	↔ paroxetine expected	No dose adjustment needed
	EFV	↔ EFV and paroxetine	No dose adjustment needed
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	↓ sertraline possible	
Trazodone	DOR, RPV IM, RPV PO	↔ trazodone expected	No dose adjustment needed
	EFV, ETR	↓ trazodone possible	Monitor for therapeutic effectiveness of trazodone and titrate dose as necessary.
Tricyclic Antidepressants (e.g., amitriptyline, doxepin, nortriptyline)	DOR, EFV, ETR, RPV IM, RPV PO	↔ antidepressant expected	No dose adjustment needed
Antipsychotics			
Aripiprazole	DOR, RPV IM, RPV PO	↔ aripiprazole expected	No dose adjustment needed
	EFV, ETR	↓ 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

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	↓ 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	↓ cariprazine and ↑ or ↓ active metabolite possible	Do not coadminister.
Iloperidone	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed
	EFV, ETR	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.
Lumateperone	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed
	EFV, ETR	↓ antipsychotic possible	Do not coadminister.
Lurasidone	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed
	EFV, ETR	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.
Olanzapine, Olanzapine/Samidorphan	DOR, ETR, 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, haloperidol, perphenazine, risperidone, thioridazine)	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed
	EFV, ETR	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.
Pimavanserin	DOR, RPV IM, RPV PO	↔ pimavanserin expected	No dose adjustment needed
	EFV, ETR	↓ pimavanserin expected	Do not coadminister.
Pimozide	DOR, RPV IM, RPV PO	↔ pimozide 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	↓ pimozide possible	Monitor for therapeutic effectiveness of pimozide.
Quetiapine	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed
	EFV, ETR	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.
Ziprasidone	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed
	EFV, ETR	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.
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
	RPV IM, RPV PO	↑ RPV possible	No dose adjustment needed. If coadministered, consider monitoring for QTc prolongation.
Ibrexafungerp	DOR, RPV PO	↑ NNRTI possible	No dose adjustment needed
	EFV, ETR	↓ ibrexafungerp expected ↑ NNRTI possible	Do not coadminister.
	RPV IM	↔ ibrexafungerp expected ↔ RPV IM expected	No dose adjustment needed
Isavuconazole	DOR	↑ DOR possible	No dose adjustment needed
	EFV, ETR	↓ isavuconazole possible	Monitor isavuconazole concentration and antifungal response. Dose adjustments for isavuconazole may be necessary.

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	No dose adjustment needed. If coadministered, consider monitoring for QTc prolongation.
Itraconazole	DOR	↑ DOR possible	No dose adjustment needed
	EFV	EFV With Itraconazole Solution • Itraconazole and OH-itraconazole AUC, C_{max}, and C_{min} ↓ 37% to 44% EFV With Itraconazole Capsules • Itraconazole AUC ↓ 86% and OH-itraconazole AUC 84%	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.
	RPV IM, RPV PO	↑ RPV possible	No dose adjustment needed. If coadministered, consider monitoring for QTc prolongation.
Posaconazole	DOR, ETR	↑ 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.
Voriconazole	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
	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
	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.
Atovaquone/Proguanil	DOR, ETR, RPV IM, RPV PO	No data	Monitor for antimalarial efficacy.
	EFV	Atovaquone AUC ↓ 75% Proguanil AUC ↓ 43%	No dose recommendation. Consider alternative drug for malaria prophylaxis, if possible.
Antimigraine			
Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonists			
Atogepant	DOR RPV IM, RPV PO	↔ atogepant expected	No dose adjustment needed
	EFV, ETR,	↓ atogepant possible	Episodic migraine: Increase atogepant dose to 30–60 mg once daily. Chronic migraine: 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
Rimegepant	DOR, RPV IM, RPV PO	↔ rimegepant expected	No dose adjustment needed
	EFV, ETR,	↓ rimegepant possible	Consider alternative ARV or migraine medication.
Ubrogepant	DOR, RPV IM, RPV PO	↔ ubrogepant expected	No dose adjustment needed
	EFV, ETR	↓ ubrogepant expected	Use initial dose of 100 mg, followed by second dose of 100 mg if needed.
Zavegepant	DOR, RPV IM, RPV PO	↔ zavegepant expected	No dose adjustment needed
	EFV, ETR,	↓ zavegepant possible	
Serotonin 5-HT1B, 1D Receptor Agonists			
Almotriptan, Eletriptan	DOR RPV IM, RPV PO	↔ almotriptan expected	No dose adjustment needed
	EFV, ETR,	↓ almotriptan possible	
Frovatriptan, Naratripan, Rizatriptan, Sumatriptan, Zolmitriptan	DOR, EFV, ETR, RPV IM, RPV PO	↔ migraine medication expected	No dose adjustment needed
Antiplatelets			
Clopidogrel	DOR, 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	↓ ticagrelor expected	Consider alternative ARV or anticoagulant therapy.
Vorapaxar	DOR, RPV IM, RPV PO	↔ vorapaxar expected	No dose adjustment needed
	EFV, ETR	↓ vorapaxar expected	Insufficient data to make a dose recommendation.
Antipneumocystis and Antitoxoplasmosis			
Atovaquone (oral solution)	DOR, ETR, RPV IM, RPV PO	No data	Monitor for therapeutic effectiveness of atovaquone.

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 ↓ 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—Hepatitis C			
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	↓ 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.
	ETR	↓ glecaprevir and pibrentasvir possible	Do not coadminister.
	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	

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	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	↓ 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	↓ voxilaprevir expected ↓ velpatasvir expected	Do not coadminister.
Antivirals—Miscellaneous (e.g., for CMV, Mpox)			
Brincidofovir	All NNRTIs	↔ brincidofovir expected	No dose adjustment needed
Cidofovir	All NNRTIs	↔ cidofovir expected	No dose adjustment needed
Maribavir	DOR, RPV IM, RPV PO	↔ maribavir expected	No dose adjustment needed
	EFV, ETR	↓ maribavir possible	
Tecovirimat	DOR, RPV PO	↓ DOR or RPV expected but not likely to be clinically relevant	No dose adjustment needed
	EFV, ETR	↔ EFV or ETR expected	No dose adjustment needed
	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 or within 2 weeks after tecovirimat treatment. (Refer to Table 24d for interaction with CAB.)

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
Antivirals—SARS-CoV-2			
Molnupiravir	All NNRTIs	↔ expected	No dose adjustment needed
Remdesivir	All NNRTIs	↔ expected	No dose adjustment needed
Ritonavir-Boosted Nirmatrelvir	DOR	With Ritonavir 100 mg Twice Daily • DOR AUC ↑ 254%	No dose adjustment needed
	EFV, ETR, RPV PO, RPV IM	↔ expected	No dose adjustment needed
Cardiac Medications			
Beta-Blockers			
Atenolol, Metoprolol, Nebivolol	DOR, EFV, ETR, RPV IM, RPV PO	↔ beta-blocker expected	No dose adjustment needed
Bisoprolol, Carvedilol	DOR, RPV IM, RPV PO	↔ beta-blocker expected	No dose adjustment needed
	EFV, ETR	↓ beta-blocker possible	No dose adjustment needed. Monitor blood pressure and heart rate and titrate to clinical effect.
Labetalol	DOR, RPV IM, RPV PO	↔ beta-blocker expected	No dose adjustment needed
	EFV, ETR	↑ beta-blocker possible	No dose adjustment needed. Monitor blood pressure and heart rate and adjust dose to achieve desired clinical effect.
Calcium Channel Blockers			
Dihydropyridine Calcium Channel Blockers (e.g., amlodipine, nifedipine)	DOR, RPV IM, RPV PO	↔ CCBs expected	No dose adjustment needed
	EFV, ETR	↓ CCBs possible	Titrate CCB dose based on clinical response.
Non-Dihydropyridine Calcium Channel Blockers (e.g., 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	↓ diltiazem or verapamil possible	

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
Cardiac—Other			
Bosentan	DOR	↓ DOR possible	Consider alternative ARV or alternative to bosentan. If coadministration is necessary, monitor virologic response.
	EFV, ETR	↓ 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.
Eplerenone	DOR, RPV IM, RPV PO	↔ eplerenone expected	No dose adjustment needed
	EFV, ETR	↓ eplerenone possible	Titrate eplerenone dose based on clinical response.
Ivabradine	DOR, RPV IM, RPV PO	↔ ivabradine expected	No dose adjustment needed
	EFV, ETR	↓ ivabradine expected	Contraindicated
Mavacamten	DOR, RPV IM, RPV PO	↔ mavacamten expected ↓ NNRTI possible	Consider alternative ARV or alternative to mavacamten. If coadministration is necessary, monitor virologic response.
	EFV, ETR	↓ mavacamten expected ↓ NNRTI possible	Contraindicated
Ranolazine	DOR, RPV IM, RPV PO	↔ ranolazine expected	No dose adjustment needed
	EFV, ETR	↓ ranolazine expected	Contraindicated
Corticosteroids			
Beclomethasone, Ciclesonide	DOR, EFV, ETR, RPV IM, RPV PO	↔ corticosteroid expected	No dose adjustment needed
Budesonide, Fluticasone, Mometasone	DOR, RPV IM, RPV PO	↔ corticosteroid 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,	↓ corticosteroid possible	Monitor corticosteroid efficacy and titrate as needed. May consider alternative corticosteroid for long-term use.
Dexamethasone	DOR, EFV, ETR	↓ 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.
Prednisone, Prednisolone	DOR, RPV IM, RPV PO	↔ corticosteroid expected	No dose adjustment needed
	EFV, ETR,	↓ corticosteroid possible	Monitor corticosteroid efficacy and titrate as needed. May consider alternative corticosteroid for long-term use.
Glucose-Lowering			
Linagliptin, Sitagliptin	DOR, RPV IM, RPV PO	↔ antihyperglycemic expected	No dose adjustment needed
	EFV, ETR	↓ antihyperglycemic possible	Monitor glycemic control.
Metformin	DOR	↔ metformin AUC DOR AUC ↓ 26% and C_{max} ↓ 24%	No dose adjustment needed
	EFV, ETR, RPV IM	↔ metformin expected	No dose adjustment needed
	RPV PO	↔ metformin AUC	No dose adjustment needed
Sodium-Glucose Cotransporter-2 Inhibitors (e.g., canagliflozin, dapagliflozin, empagliflozin)	DOR, EFV, ETR, RPV IM, RPV PO	↔ antihyperglycemic expected	No dose adjustment needed
Herbal Products			
St. John's Wort	DOR	↓ DOR expected	**Contraindicated.** After stopping St. John's Wort, wait 4 weeks before initiating DOR.
	EFV, ETR	↓ EFV or ETR expected	Do not coadminister.
	RPV IM, RPV PO	↓ RPV expected	Contraindicated

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
Hormonal Therapies—Contraceptives			
Injectable Contraceptives Depot MPA	DOR, ETR, RPV IM, RPV PO	↔ MPA expected	No dose adjustment needed
	EFV	↔ MPA	No dose adjustment needed. Refer to Women With HIV section for people on EFV and RIF.
Oral Contraceptives (e.g., desogestrel, drospirenone, ethinyl estradiol, levonorgestrel, norgestimate)	DOR	↔ ethinyl estradiol ↔ levonorgestrel ↔ drospirenone expected	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% ↓ drospirenone possible	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 ↓ drospirenone possible	No dose adjustment needed for regimens that do not contain drospirenone For drospirenone-containing regimens used for contraception, use alternative ARV or alternative contraceptive method. If using drospirenone for other clinical indications, monitor for clinical effectiveness of hormonal therapy.
	RPV IM	↔ ethinyl estradiol expected ↔ norethindrone expected ↔ drospirenone 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 PO	↔ ethinyl estradiol ↔ norethindrone ↔ drospirenone expected	No dose adjustment needed
Subdermal Implant Contraceptives (e.g., etonogestrel, levonorgestrel)	DOR, RPV IM, RPV PO	↔ etonogestrel expected ↔ levonorgestrel expected	No dose adjustment needed
	EFV	Etonogestrel AUC ↓ 63% to 82% Levonorgestrel AUC ↓ 42% to 47% Levonorgestrel 300 mg Implant With 600 mg EFV Compared to Levonorgestrel 150 mg Implant • Levonorgestrel AUC ↓ 34%	Use alternative ARV or contraceptive methods. Unintended pregnancies were observed in women who used EFV and levonorgestrel implant concomitantly.
	ETR	↓ etonogestrel possible ↓ levonorgestrel possible	Consider using alternative ARV or contraceptive methods.
Transdermal Contraceptives (e.g., ethinyl estradiol/norelgestromin, ethinyl estradiol/levonorgestrel)	DOR, RPV IM, RPV PO	↔ ethinyl estradiol or norelgestromin expected	No dose adjustment needed
	EFV	↓ ethinyl estradiol or norelgestromin possible	Consider alternative ARV or contraceptive method.
	ETR	↓ ethinyl estradiol or norelgestromin possible	Consider alternative ARV or contraceptive method.
Vaginal Ring Contraceptives (e.g., etonogestrel/ethinyl estradiol, segesterone/ethinyl estradiol)	DOR, RPV IM, RPV PO	↔ etonogestrel and ethinyl estradiol expected ↔ segesterone and ethinyl estradiol expected	No dose adjustment needed
	EFV	Ethinyl estradiol (intravaginal ring) AUC ↓ 56% Etonogestrel (intravaginal ring) AUC ↓ 81%	Use alternative ARV or contraceptive method.
		↓ segesterone and ethinyl estradiol possible	Consider alternative ARV or contraceptive method.
	ETR	↓ etonogestrel and ethinyl estradiol possible ↓ segesterone and ethinyl estradiol possible	Consider alternative ARV or contraceptive method.

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
Emergency Contraceptives Levonorgestrel (oral)	DOR, RPV IM, RPV PO	↔ levonorgestrel expected	No dose adjustment needed.
	EFV	Levonorgestrel 1.5 mg Plus 600 mg EFV • Levonorgestrel AUC ↓ 58% Levonorgestrel 3 mg Plus 600 mg EFV Compared to Levonorgestrel 1.5 mg Alone • ↔ levonorgestrel AUC	Increase dose of levonorgestrel to 3mg when used for emergency postcoital contraception.
	ETR	↓ levonorgestrel possible	Consider alternative ARV or contraceptive method.
Hormonal Therapies—Gender Affirming and Menopause			
Estradiol	DOR, RPV IM, RPV PO	↔ estradiol expected	No dose adjustment needed
	EFV	Estradiol AUC ↓ 28% ↔ EFV AUC	Monitor feminizing effects of estrogen and therapy. Titrate dose as necessary to achieve therapeutic goals
	ETR	↓ estradiol possible	
5-Alpha Reductase Inhibitors (e.g., dutasteride, finasteride)	DOR, RPV IM, RPV PO	↔ dutasteride and finasteride expected	No dose adjustment needed
	EFV, ETR	↓ dutasteride and finasteride possible	Monitor masculinizing effects of testosterone. Titrate testosterone dose as necessary to achieve therapeutic goals.
Testosterone	DOR, RPV IM, RPV PO	↔ testosterone expected	No dose adjustment needed
	EFV, ETR	↓ testosterone possible	Monitor masculinizing effects of testosterone. Titrate testosterone dose as necessary to achieve therapeutic goals.
Other Gender-Affirming Medications	DOR, RPV IM, RPV PO	↔ hormonal concentrations expected	No dose adjustment needed
	EFV, ETR	↓ cyproterone and progestogens possible ↔ goserelin, leuprolide acetate, and spironolactone expected	Monitor feminizing effects of estrogen and antiandrogen therapy. Titrate dose as necessary to achieve therapeutic goals.

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
Menopausal Hormone Replacement Therapy (e.g., conjugated estrogens, drospirenone, estradiol, medroxyprogesterone, progesterone)	DOR, RPV IM, RPV PO	↔ hormonal concentrations expected	No dose adjustment needed
	EFV, ETR	↓ 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	↓ 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	↓ immunosuppressant possible	Increase in immunosuppressant dose may be necessary. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with specialist as necessary.
Lipid-Modifying			
Atorvastatin	DOR	↔ atorvastatin AUC	No dose adjustment needed
	EFV, ETR	Atorvastatin AUC ↓ 32% to 43%	Adjust atorvastatin dose according to lipid response, but do not exceed the maximum recommended dose.

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	↔ atorvastatin expected	No dose adjustment needed
	RPV PO	↔ atorvastatin AUC	No dose adjustment needed
Fluvastatin	DOR, 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	↓ lovastatin possible ↓ simvastatin possible	Adjust lovastatin or simvastatin dose according to lipid response, but do not exceed the maximum recommended dose.
Pitavastatin	DOR, ETR, RPV IM, RPV PO	↔ pitavastatin expected	No dose adjustment needed
	EFV	↔ pitavastatin AUC	No dose adjustment needed
Pravastatin	DOR, 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, RPV IM, RPV PO	↔ rosuvastatin expected	No dose adjustment needed
Narcotics and Treatment for Opioid Dependence			
Buprenorphine Sublingual or buccal	DOR, RPV IM, RPV PO	↔ buprenorphine expected	No dose adjustment needed
	EFV	Buprenorphine AUC ↓ 50% Norbuprenorphine (active metabolite) AUC ↓ 71%	No dose adjustment needed, monitor for withdrawal symptoms.

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	Buprenorphine AUC ↓ 25%	No dose adjustment needed
Buprenorphine Implant	DOR, RPV IM, RPV PO	↔ buprenorphine expected	No dose adjustment needed
	EFV, ETR	No data	Clinical monitoring is recommended when NNRTI is initiated after insertion of buprenorphine implant.
Lofexidine	DOR, EFV, ETR, 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
	RPV IM	↓ methadone AUC expected	No dose adjustment needed; monitor for withdrawal symptoms.
	RPV PO	↔ R-methadone[a] AUC	No dose adjustment needed; monitor for withdrawal symptoms.
PDE5 Inhibitors			
Avanafil, Tadalafil, Vardenafil	DOR, RPV IM, RPV PO	↔ PDE5 inhibitor expected	No dose adjustment needed
	EFV, ETR	↓ PDE5 inhibitor possible	May need to titrate dose based on clinical effect.
Sildenafil	DOR	↔ sildenafil expected	No dose adjustment needed
	EFV	↓ 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

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
Sedative/Hypnotics			
Benzodiazepines			
Alprazolam, Triazolam	DOR, RPV IM, RPV PO	↔ alprazolam or triazolam expected	No dose adjustment needed
	EFV, ETR	↓ alprazolam or triazolam possible	Monitor for therapeutic effectiveness of benzodiazepine.
Diazepam	DOR, RPV IM, RPV PO	↔ diazepam expected	No dose adjustment needed
	EFV	↓ 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, 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.
	RPV IM, RPV PO	↔ midazolam expected	No dose adjustment needed
Orexin Receptor Antagonists			
Daridorexant	DOR, RPV IM, RPV PO	↔ daridorexant expected	No dose adjustment needed
	EFV	Daridorexant AUC ↓ 61%	Do not coadminister.
	ETR	↓ daridorexant possible	
Lemborexant, Suvorexant	DOR, RPV IM, RPV PO	↔ lemborexant expected	No dose adjustment needed
	EFV, ETR	↓ lemborexant possible	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
Other Sedatives			
Eszopiclone, Zolpidem	DOR, RPV IM, RPV PO	↔ eszopiclone or zolpidem expected	No dose adjustment needed
	EFV, ETR	↓ eszopiclone or zolpidem possible	Monitor for therapeutic effectiveness of sedative and titrate to clinical effect.
Miscellaneous			
Finerenone	DOR, RPV IM, RPV PO	↔ finerenone expected	No dose adjustment needed
	EFV, ETR	↓ finerenone expected	Consider alternative ARV or alternative to finerenone. If coadministration is necessary, monitor finerenone efficacy.
Praziquantel	DOR, RPV IM, RPV PO	↔ praziquantel expected	No dose adjustment needed
	EFV	R-praziquantel and S-praziquantel AUC ↓ 74% to 75%	Do not coadminister. If coadministration is necessary, consider alternative ARVs.
	ETR	↓ praziquantel possible	Do not coadminister. If coadministration is necessary, consider alternative ARVs.

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

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

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; DOAC = direct oral anticoagulants; DOR = doravirine; EFV = efavirenz; ETR = etravirine; IM = intramuscular; INR = international normalized ratio; isoniazid = isonicotinic acid hydrazide; MAC = *Mycobacterium avium* complex; MPA = medroxyprogesterone acetate; CMV = cytomegalovirus; NNRTI = non-nucleoside reverse transcriptase inhibitor; 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

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

Updated: September 12, 2024
Reviewed: September 12, 2024

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 judgment to select the most appropriate alternative medication.

This table focuses on interactions with pharmacokinetic study data and interactions without study data but where there is a clinical recommendation. Interactions associated with zidovudine (ZDV) are **not** included in this table. Please refer to the U.S. Food and Drug Administration product labels for information regarding drug interactions between ZDV and other drugs.

Concomitant Drug	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antibacterials—Antimycobacterials			
Rifabutin	3TC, ABC, FTC,	↔ expected	No dose adjustment needed
	TAF	↓ TAF possible	Use with caution. If coadministered, monitor virologic response.
	TDF	↔ AUC TFV	No dose adjustment needed
Rifampin	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	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	Use with caution. If coadministered, monitor virologic response. 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.

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
		• TAF AUC ↓ 14% • TFV-DP AUC ↓ 24%	
	TDF	↔ AUC TFV	No dose adjustment needed
Rifapentine	3TC, ABC, FTC,	↔ expected	No dose adjustment needed
	TAF	↓ TAF possible	Use with caution. If coadministered, monitor virologic response.
	TDF	↔ AUC TFV	No dose adjustment needed
Antiseizure			
Carbamazepine, Oxcarbazepine, Phenobarbital, Phenytoin	ABC	↑ carbamazepine possible ↓ ABC possible with oxcarbazepine, phenobarbital, phenytoin	No dose adjustment needed
	3TC, FTC, TDF	↔ expected	No dose adjustment needed
	TAF	With Carbamazepine • TAF AUC ↓ 55% • ↓ TAF possible with other anticonvulsants	Do not coadminister.
Antivirals—Hepatitis C			
Glecaprevir/Pibrentasvir	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	↔ TFV AUC	No dose adjustment needed
	TDF	TFV AUC ↑ 29%	No dose adjustment needed
Ledipasvir/Sofosbuvir	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	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	3TC	↔ 3TC AUC	No dose adjustment needed
	ABC, FTC, TAF	↔ expected	No dose adjustment needed
	TDF	Ribavirin With Sofosbuvir 400 mg • ↔ TFV AUC	No dose adjustment needed
Sofosbuvir/Velpatasvir	3TC, ABC, FTC, TAF	↔ 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	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	TAF AUC ↑ 52% to 57%	No dose adjustment needed
	TDF	TFV C_{max} ↑ 48% and AUC ↑ 39% when coadministered with various ARV combinations.	Monitor for TDF-related toxicities. Consider using TAF in patients at risk of TDF-related adverse events.
Antivirals—Miscellaneous (e.g., for Herpesvirus, CMV, HBV, Mpox)			
Adefovir	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	↑ TFV possible	Do not coadminister. Serum concentrations of TDF and/or other renally eliminated drugs may increase.

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	↔ TFV	Do not coadminister.
Brincidofovir	3TC, ABC, FTC, TAF, TDF	↔ brincidofovir expected	No dose adjustment needed
Cidofovir	3TC, ABC, 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.
Famciclovir	3TC, ABC, TAF, TDF	↔ expected	No dose adjustment needed
	FTC	↔ AUC FTC, famciclovir	No dose adjustment needed
Ganciclovir, Valganciclovir	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF, TDF	↑ ganciclovir or TFV possible	Monitor for dose-related toxicities.
Tecovirimat	3TC, ABC, FTC, TAF, TDF	↔ tecovirimat expected	No dose adjustment needed
Antivirals—SARS-CoV-2			
Molnupiravir	3TC, ABC, FTC, TAF, TDF	↔ expected	No dose adjustment needed
Remdesivir	3TC, ABC, FTC, TAF, TDF	↔ expected	No dose adjustment needed
Ritonavir-Boosted Nirmatrelvir	3TC, ABC, FTC, TAF, TDF	↔ 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
Hormonal Therapies—Contraceptives			
Injectable Contraceptives Depot MPA	3TC, ABC, TAF	↔ expected	No dose adjustment needed
	FTC, TDF	↔ FTC AUC ↔ TFV AUC	No dose adjustment needed
Oral Contraceptives (e.g., desogestrel, drospirenone, ethinyl estradiol, levonorgestrel, norelgestromin, norgestimate, norgestrel)	3TC, ABC, FTC, TDF	↔ expected	No dose adjustment needed
	TAF	↔ ethinyl estradiol AUC ↔ norelgestromin AUC ↔ norgestrel AUC	No dose adjustment needed
Hormonal Therapies—Gender Affirming and Menopause			
Estradiol Valerate	3TC, ABC, TAF	↔ expected	No dose adjustment needed
	FTC	↔ FTC AUC ↔ estradiol AUC	
	TDF	↔ TFV AUC ↔ estradiol	
17-β-estradiol	3TC, ABC, TAF	↔ expected	No dose adjustment needed
	FTC	FTC AUC ↓ 14% to 24%	
	TDF	TFV AUC ↓ 12% to 27%	
Other Medications Used for Gender-Affirming Therapy or Menopausal Replacement Therapy	ABC, 3TC, FTC, TAF, TDF	↔ NRTI expected	No dose adjustment needed
Narcotics and Treatment for Opioid Dependence			
Buprenorphine	ABC, FTC	↔ expected	No dose adjustment needed
	3TC, TDF	↔ 3TC, TDF, and buprenorphine	No dose adjustment needed
	TAF	↔ TAF 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
Methadone	3TC, FTC, TAF, TDF	↔ expected	No dose adjustment needed
	ABC	Methadone clearance ↑ 22%	No dose adjustment needed
Miscellaneous			
Ethanol	ABC	ABC AUC ↑ 41%	No dose adjustment needed
Riociguat	3TC, FTC, TAF, TDF	↔ expected	No dose adjustment needed
	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	3TC, ABC, FTC, TDF	↔ expected	No dose adjustment needed
	TAF	↓ TAF possible	Do not coadminister.
Antiretrovirals			
Capsid Inhibitor			
LEN (SQ and PO)	3TC, ABC, FTC	↔ 3TC, ABC, FTC, 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	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	↔ TAF AUC	No dose adjustment needed
	TDF	↔ TDF AUC ↔ DTG AUC	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
RAL	3TC, ABC, FTC, TAF	↔ expected	No dose adjustment needed
	TDF	RAL AUC ↑ 49%	No dose adjustment needed
PIs			
ATV/c, ATV/r	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	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%	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 patient, use ATV 400 mg plus (RTV 100 mg or COBI 150 mg) daily. Monitor for TDF-associated toxicities.
DRV/c	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	TAF 25 mg With DRV/c • ↔ TAF	No dose adjustment needed
	TDF	TFV ↑ possible	Monitor for TDF-associated toxicities.
DRV/r	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	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.

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir;

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

ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; C_{max} = maximum plasma concentration; C_{min} = minimum plasma concentration; COBI = cobicistat; CMV = cytomegalovirus; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; HBV = hepatitis B virus; HCV = hepatitis C virus; INSTI = integrase strand transfer inhibitor; LEN = lenacapavir; MPA = medroxyprogesterone acetate; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; PO: oral; 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

Updated: September 12, 2024
Reviewed: September 12, 2024

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 drugs. EVG is always coadministered with cobicistat (COBI or c). 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. Because drug interaction studies were not conducted with either IM CAB or RPV, dosing recommendations for the IM formulations are based on drug interaction studies using oral CAB and RPV. For information regarding interactions between INSTIs and other antiretroviral (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 judgment to select the most appropriate alternative medication.

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.

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 ↓ 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
	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

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	↑ 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. Monitor blood pressure. Doxazosin dose reduction may be needed.
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 blood pressure.
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. Monitor blood pressure. 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			
Bedaquiline	BIC, CAB (PO and IM), DTG, RAL	↔ bedaquiline	No dosage adjustment needed
	EVG/c	↑ bedaquiline possible	Do not coadminister unless benefits outweigh risks. If coadministered, consider therapeutic drug monitoring and monitor for bedaquiline-related adverse effects, including hepatotoxicity and QTc prolongation.
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.

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	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 and C_{min} ↓ 20%	No dose adjustment needed
Rifampin	BIC	BIC AUC ↓ 75%	Contraindicated
	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	Significant ↓ CAB (PO and IM)	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
	IM)	expected	
	DTG	Rifapentine 900 mg Once Weekly • DTG AUC ↓ 26% and C_{min} ↓ 47% Rifapentine 600 mg Once Daily With DTG 50 mg Twice Daily vs DTG 50 mg Once Daily Alone • ↔ DTG AUC and C_{min}	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. With once-daily rifapentine for 4 weeks (1HP), use DTG 50 mg twice daily. See Tuberculosis/HIV Coinfection for more on rifapentine and DTG use.
	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.
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

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	↑ 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%	Reduction of Risk of Stroke and Systemic Embolism in Nonvalvular Atrial Fibrillation in Adult Patients • CrCl >30 mL/min: no dose adjustment needed • CrCl ≤30 mL/min: do not coadminister. Treatment and Reduction in the Risk of Recurrence of DVT and PE or Prophylaxis of DVT and PE Following Hip Replacement Surgery in Adult Patients • CrCl ≥50 mL/min: no dose adjustment needed • CrCl <50 mL/min: do not coadminister.
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 DVT and PE • Administer edoxaban 30 mg once daily.
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.
Antiseizure			
Carbamazepine	BIC	↓ BIC possible	Do not coadminister.
	CAB (PO and IM)	↓ CAB 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
	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, Primidone	BIC, DTG, RAL	↓ BIC and DTG possible ↓ or ↔ RAL possible	Do not coadminister.
	CAB (PO and IM), EVG/c	↓ CAB and EVG/c expected	Contraindicated
Valproic Acid	DTG	DTG ↓ possible	No dose adjustment needed. Take with food and monitor virologic response.
	BIC, CAB (PO and IM), RAL	No data	No dose adjustment needed. Monitor virologic response.

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
Antidepressants, Anxiolytics, and Antipsychotics Also see the Sedative/Hypnotics section below			
Antidepressants, Anxiolytics			
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.
Desvenlafaxine	All INSTIs	↔ desvenlafaxine expected	No dose adjustment needed
Duloxetine	BIC, CAB (PO and IM), DTG, RAL	↔ duloxetine expected	No dose adjustment needed
	EVG/c	↑ duloxetine possible	No dose adjustment needed
Mirtazapine	BIC, CAB (PO and IM), DTG, RAL	↔ mirtazapine expected	No dose adjustment needed
	EVG/c	↑ mirtazapine possible	Monitor for mirtazapine-related adverse events. Mirtazapine dose reduction may be necessary.
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
	EVG/c	↑ trazodone possible	Titrate dose based on antidepressant response and monitor for trazodone-related adverse events.

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
Tricyclic Antidepressants (e.g., 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 (e.g., citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, vortioxetine)	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
Venlafaxine	BIC, CAB (PO and IM), DTG, RAL	↔ venlafaxine expected	No dose adjustment needed
	EVG/c	↑ venlafaxine possible	Monitor for venlafaxine-related adverse events.
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 effectiveness and adverse events. Refer to aripiprazole label for dosing recommendations in patients who are known to be CYP2D6-poor metabolizers or who have major depressive disorder.
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 effectiveness 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

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	↑ 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, Olanzapine/ Samidorphan	All INSTIs	↔ olanzapine expected	No dose adjustment needed
	EVG/c	↔ olanzapine expected ↑ samidorphan possible	No dose adjustment needed
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

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	↑ 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.
Antimigraine			
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
Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonists			
Atogepant	BIC, CAB (PO and IM), DTG, RAL	↔ atogepant expected ↑ atogepant expected	No dose adjustment needed
	EVG/c	↑ atogepant expected	Chronic migraine: Do not coadminister. Episodic migraine: Administer atogepant at a dose of 10 mg once daily.
Rimegepant	BIC, CAB (PO and IM), DTG, RAL	↔ rimegepant 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	↑ rimegepant expected	Do not coadminister.
Ubrogepant	BIC, CAB (PO and IM), DTG, RAL	↔ ubrogepant expected	No dose adjustment needed
	EVG/c	↑ ubrogepant expected	Contraindicated
Zavegepant	BIC, CAB (PO and IM), DTG, RAL	↔ zavegepant expected	No dose adjustment needed
	EVG/c	↑ zavegepant expected	Do not coadminister.
Serotonin 5-HT1B, 1D Receptor Agonist			
Almotriptan	BIC, CAB (PO and IM), DTG, RAL	↔ almotriptan expected	No dose adjustment needed
	EVG/c	↑ almotriptan expected	Administer single dose of almotriptan 6.25 mg. Maximum dose should not exceed 12.5 mg in a 24-hour period.
Eletriptan	BIC, CAB (PO and IM), DTG, RAL	↔ eletriptan expected	No dose adjustment needed
	EVG/c	↑ eletriptan expected	Contraindicated
Frovatriptan, Naratriptan, Rizatriptan, Sumatriptan Zolmitriptan	All INSTIs	↔ triptan expected	No dose adjustment needed
Antifungals			
Ibrexafungerp	BIC, CAB (PO and IM), DTG, RAL	↔ ibrexafungerp expected	No dose adjustment needed
	EVG/c	↑ ibrexafungerp expected	Reduce ibrexafungerp dose to 150 mg twice daily.
Isavuconazole	BIC, CAB (PO and IM), DTG, RAL	↑ INSTI possible	No dose adjustment needed
	EVG/c	↑ isavuconazole expected ↑ or ↓ EVG and COBI possible	Contraindicated
Itraconazole	BIC	↑ BIC expected	No dose adjustment needed
	CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ itraconazole 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	↑ itraconazole expected ↑ EVG and COBI possible	Consider monitoring itraconazole concentrations to guide dose adjustments. Do not coadminister with high itraconazole doses (>200 mg/day) unless guided by itraconazole concentrations.
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.
Antimalarials			
Artemether/ Lumefantrine	BIC	↔ antimalarial expected	No dose adjustment needed
	CAB (PO and IM), DTG, RAL	↔ antimalarial expected	No dose adjustment needed
	EVG/c	↑ artemether and lumefantrine possible	Monitor for artemether and lumefantrine-related adverse events, including QTc prolongation.
Artesunate	All INSTIs	↔ dihydroartemisinin expected	No dose adjustment needed
Atovaquone/ Proguanil	All INSTIs	↔ atovaquone/proguanil expected	No dose adjustment needed
Mefloquine	CAB (PO and IM), DTG, RAL	↔ mefloquine expected	No dose adjustment needed
	EVG/c	↑ mefloquine possible	Monitor for mefloquine-related adverse events, including psychiatric symptoms and QTc prolongation.
Glucose-Lowering			
Metformin	BIC	Metformin AUC ↑ 39%	Monitor for adverse events of metformin.
	CAB (PO and IM), RAL	↔ metformin 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 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.
	EVG/c	↑ metformin possible	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.
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.

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
Vorapaxar	BIC, CAB (PO and IM) DTG, RAL	↔ vorapaxar expected	No dose adjustment needed
	EVG/c	↑ vorapaxar expected	Do not coadminister.
Antipneumocystis and Antitoxoplasmosis			
Atovaquone	All INSTIs	↔ atovaquone expected	No dose adjustment needed
Antivirals—Hepatitis C			
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

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/TDF/FTC	↑ TDF expected ↑ ledipasvir expected	Do not coadminister.
	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
Antivirals—Miscellaneous (e.g., for CMV, Mpox)			
Brincidofovir	BIC, CAB (PO and IM), DTG, RAL	↔ INSTI 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	↑ brincidofovir possible ↑ EVG possible	Administer EVG/c dose at least 3 hours after administering brincidofovir and monitor for brincidofovir-related adverse events, including elevations in ALT/AST and bilirubin and GI adverse events.
Cidofovir	BIC, CAB (PO and IM), DTG, EVG/c, 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
Antivirals—SARS-CoV-2			
Molnupiravir	BIC, CAB (PO and IM), DTG, EVG/c, RAL	↔ INSTI and molnupiravir expected	No dose adjustment needed
Ritonavir-boosted Nirmatrelvir	BIC, CAB (PO and IM), DTG, RAL	↔ INSTI and ritonavir-boosted nirmatrelvir expected	No dose adjustment needed.
	EVG/c/FTC/TAF	↑ TAF possible ↔ ritonavir-boosted nirmatrelvir expected	No dose adjustment needed
Remdesivir	BIC, CAB (PO and IM), DTG, EVG/c, RAL	↔ INSTI and remdesivir expected	No dose adjustment needed
Beta-Agonists, Long-Acting Inhaled			
Arformoterol, Formoterol	All INSTIs	↔ arformoterol or formoterol expected	No dose adjustment needed
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	

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
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			
Antiarrhythmics			
Amiodarone	BIC, CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ amiodarone expected	No dose adjustment needed
	EVG/c	↑ amiodarone expected	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.
Digoxin	BIC, CAB (PO and IM), RAL	↔ digoxin expected	No dose adjustment needed
	EVG/c	Digoxin C_{max} ↑ 41% and ↔ AUC	Therapeutic drug monitoring for digoxin is recommended if available.
Dofetilide	CAB (PO and IM)	↔ dofetilide expected	No dose adjustment needed
	BIC, DTG	↑ dofetilide expected	Contraindicated
	EVG/c	↑ dofetilide possible	Do not coadminister.
Disopyramide	BIC, CAB (PO and IM), RAL	↔ disopyramide expected	No dose adjustment needed
	DTG	↑ disopyramide possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor disopyramide concentrations and for antiarrhythmic-related adverse events.
	EVG/c	↑ disopyramide expected	Do not coadminister.
Dronedarone	BIC, CAB (PO and IM), DTG, RAL	↔ dronedarone expected	No dose adjustment needed
	EVG/c	↑ dronedarone expected	Contraindicated
Flecainide	BIC, CAB (PO and IM), DTG, RAL	↔ flecainide expected	No dose adjustment needed
	EVG/c	↑ flecainide possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor flecainide concentrations and for antiarrhythmic-related adverse events.

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
Propafenone	BIC, CAB (PO and IM), DTG, RAL	↔ propafenone expected	No dose adjustment needed
	EVG/c	↑ propafenone possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor propafenone concentrations and for antiarrhythmic-related adverse events.
Mexiletine	BIC, CAB (PO and IM), DTG, RAL	↔ mexiletine expected	No dose adjustment needed
	EVG/c	↑ mexiletine possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor mexiletine concentrations and for antiarrhythmic-related adverse events.
Systemic Lidocaine	BIC, CAB (PO and IM), DTG, RAL	↔ lidocaine expected	No dose adjustment needed
	EVG/c	↑ lidocaine possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor lidocaine concentrations and for antiarrhythmic-related adverse events.
Quinidine	BIC, CAB (PO and IM), DTG, RAL	↔ quinidine expected	No dose adjustment needed
	EVG/c	↑ quinidine possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor quinidine concentrations and for antiarrhythmic-related adverse events.
Beta-Blockers			
Atenolol, Bisoprolol, Carvedilol, Metoprolol, Nadolol, Nebivolol, Sotalol	CAB (PO and IM), RAL	↔ beta-blocker expected	No dose adjustment needed
	BIC, DTG, EVG/c	↑ beta-blocker possible	Beta-blocker dose may need to be decreased; adjust dose based on clinical response.
Calcium Channel Blockers			
Calcium Channel Blockers	BIC	↑ BIC possible with diltiazem ↔ expected for all other CCBs	No dose adjustment needed
	CAB (PO and IM), DTG, RAL	↔ CCB expected	No dose adjustment needed
	EVG/c	↑ CCB possible	Titrate CCB dose and monitor for CCB efficacy and adverse events.

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
Cardiac—Other			
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 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.
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
Mavacamten	BIC, CAB (PO and IM), DTG, RAL	↔ mavacamten expected	No dose adjustment needed
	EVG/c	↑ mavacamten expected	Contraindicated
Ranolazine	BIC, CAB (PO and IM), DTG, RAL	↔ ranolazine expected	No dose adjustment needed
	EVG/c	↑ ranolazine 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
Corticosteroids			
Beclomethasone Inhaled or intranasal	BIC, CAB (PO and IM), DTG, EVG/c, RAL	↔ glucocorticoid expected	No dose adjustment needed
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.

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
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.
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			
Injectable Contraceptives Depot MPA	BIC, CAB (PO and IM), DTG, RAL	↔ INSTI and injectable contraceptive expected	No dose adjustment needed
	EVG/c	↑ MPA possible	No dose adjustment needed
Oral Contraceptives (e.g., desogestrel, drospirenone, ethinyl estradiol, levonorgestrel, norethindrone, norgestimate)	BIC, CAB (PO, IM), DTG, RAL	↔ ethinyl estradiol and norgestimate with DTG ↔ ethinyl estradiol and levonorgestrel with CAB PO ↔ ethinyl estradiol and norgestimate expected with BIC, RAL ↔ norgestimate expected with CAB PO and IM ↔ levonorgestrel expected ↔ drospirenone expected ↔ norethindrone expected	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.

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
		↑ levonorgestrel possible ↑ norethindrone expected	No dose adjustment needed
Subdermal Implant Contraceptives (e.g., etonogestrel, levonorgestrel)	BIC, CAB (PO and IM), DTG, RAL	Etonogestrel ↑ 27% with DTG ↔ etonogestrel or levonorgestrel expected with BIC, CAB, RAL	No dose adjustment needed
	EVG/c	↑ etonogestrel expected ↑ levonorgestrel expected	No dose adjustment needed
Transdermal Contraceptives (e.g., ethinyl estradiol/ norelgestromin, ethinyl estradiol/ levonorgestrel)	BIC, CAB (PO, IM), DTG, RAL	↔ contraceptive expected	No dose adjustment needed
	EVG/c	↑ progestin possible ↓ ethinyl estradiol possible	No dose adjustment needed
Vaginal Ring Contraceptives (e.g., etonogestrel/ ethinyl estradiol, segesterone/ethinyl estradiol)	BIC, CAB (PO, IM), DTG, RAL	↔ contraceptive expected	No dose adjustment needed
	EVG/c	↑ progestin possible ↓ ethinyl estradiol possible	For segesterone/ethinyl estradiol vaginal rings, use alternative ARV or contraceptive methods.
Emergency Contraceptives Levonorgestrel (PO)	BIC, CAB (PO, IM), DTG, RAL	↔ levonorgestrel expected	No dose adjustment needed
	EVG/c	↑ levonorgestrel possible	No dose adjustment needed
Hormonal Therapies—Gender-Affirming and Menopause			
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	↑ or ↓ 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.

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
Menopausal Replacement Therapy	BIC, CAB (PO and IM), DTG, RAL	↔ estrogen expected with estradiol or conjugated estrogen (equine and synthetic) ↔ drospirenone, MPA, and micronized progesterone expected	No dose adjustment needed
	EVG/c	↓ or ↑ estrogen possible ↑ drospirenone possible ↑ oral MPA possible ↑ oral micronized progesterone possible	Adjust estrogen and progestin dose as needed based on clinical effects.
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			
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	Administer the lowest effective dose while monitoring for adverse events. Do not exceed 20 mg atorvastatin daily.
Fluvastatin	BIC, CAB (PO and IM), DTG, RAL	↔ fluvastatin expected	No dose adjustment needed
	EVG/c	↑ fluvastatin possible	Administer the lowest effective fluvastatin dose while monitoring for adverse events.
Lomitapide	BIC, CAB (PO and IM), DTG, RAL	↔ lomitapide expected	No dose adjustment needed
	EVG/c	↑ lomitapide 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
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 dose adjustment needed. Monitor for adverse events.
Rosuvastatin	BIC, CAB (PO and IM), DTG, RAL	↔ rosuvastatin expected	No dose adjustment needed
	EVG/c	Rosuvastatin AUC ↑ 38% and C_{max} ↑ 89%	Administer 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
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.

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
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
	EVG/c	↑ sildenafil expected	For Treatment of Erectile Dysfunction • Start with sildenafil 25 mg every 48 hours and monitor for sildenafil-related adverse events. 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 tadalafil-related adverse events. 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.

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
			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 vardenafil-related adverse events.
Sedative/Hypnotics			
Benzodiazepines			
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
	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.
Orexin Receptor Antagonists			
Daridorexant, Lemborexant, Suvorexant	BIC, CAB (PO and IM), DTG, RAL	↔ daridorexant, lemborexant, suvorexant expected	No dose adjustment needed
	EVG/c	↑ daridorexant, lemborexant, suvorexant expected	Do not coadminister.
Other Sedatives			
Eszopiclone	BIC, CAB (PO and IM), DTG, RAL	↔ eszopiclone 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	↑ eszopiclone expected	Start with lowest dose and increase to a max of 2 mg daily. Monitor for eszopiclone-related adverse events.
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. 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.

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
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
Finerenone	BIC, CAB (PO and IM), DTG, RAL	↔ finerenone expected	No dose adjustment needed
	EVG/c	↑ finerenone expected	Contraindicated
Flibanserin	BIC, CAB (PO and IM), DTG, RAL	↔ flibanserin expected	No dose adjustment needed
	EVG/c	↑ flibanserin expected	Contraindicated
Naloxegol	BIC, CAB (PO and IM), DTG, RAL	↔ naloxegol expected	No dosage adjustment needed
	EVG/c	↑ naloxegol 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.

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 ↓ 39% if administered simultaneously with $CaCO_3$ under fasting conditions DTG AUC ↓ 54% if administered simultaneously with Fe under fasting conditions ↔ DTG when administered with Ca or Fe supplement simultaneously with food	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. 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.
Praziquantel	BIC, CAB (PO and IM), DTG, RAL	↔ praziquantel and INSTI expected	No dose adjustment needed
	EVG/c	↑ praziquantel possible	Consider alternative ARV. If coadministration is necessary, monitor for praziquantel-related adverse events.

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

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; CMV = cytomegalovirus; COBI = cobicistat; CrCl = creatinine clearance; CYP = cytochrome P450; DTG = dolutegravir; DVT = deep vein thrombosis; 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; MPA = medroxyprogesterone acetate; PAH = pulmonary arterial hypertension; PDE5 = phosphodiesterase type 5; PE = pulmonary embolism; PO = orally; PTH = parathyroid hormone; QTc = QT corrected for heart rate; RAL = raltegravir; RPV = rilpivirine; 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)

Updated: September 12, 2024
Reviewed: September 12, 2024

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 judgment to select the most appropriate alternative medication.

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
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
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

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
Rifapentine	Rifapentine Weekly and Daily ↓ MVC expected	Do not coadminister.
Antiseizure		
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.
Antivirals—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
Antivirals—Miscellaneous (e.g., for CMV, 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
Antivirals—SARS-CoV-2		
Molnupiravir	↔ MVC expected	No dose adjustment needed
Remdesivir	↔ MVC 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
Ritonavir-Boosted Nirmatrelvir	MVC With Ritonavir 100 mg Twice Daily • MVC AUC ↑ 161%	MVC 150 mg twice daily
Herbal Products		
St. John's Wort	↓ MVC expected	Do not coadminister.
Hormonal Therapies		
Hormonal Contraceptives	↔ ethinyl estradiol or levonorgestrel	No dose adjustment needed
Gender-Affirming Hormone Therapies	↔ MVC or gender-affirming hormones expected	No dose adjustment needed
Menopausal Hormone Replacement Therapy	↔ MVC or hormone replacement therapies expected	No dose adjustment needed
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

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
PIs		
ATV/c, ATV/r	With (ATV/r 300 mg/100 mg) Once Daily • MVC AUC ↑ 388%	MVC 150 mg twice daily.
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

[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; CMV = cytomegalovirus; 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; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; ; 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)

Updated: September 12, 2024
Reviewed: September 12, 2024

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 judgment 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 dose adjustment needed If Used *With* PI/r • Recommended dose is rifabutin 150 mg once daily. • No dose adjustment of FTR
Rifampin	TMR AUC ↓ 82%	Contraindicated
Rifapentine	Daily and Weekly Dosing ↓ TMR expected	Do not coadminister.
Antivirals—Hepatitis C Direct-Acting Antivirals		
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

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
Sofosbuvir/Velpatasvir/Voxilaprevir	↑ voxilaprevir expected	Use an alternative HCV regimen if possible.
Antivirals—Miscellaneous (e.g., for CMV, 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
Antivirals—SARS-CoV-2		
Molnupiravir	↔ expected	No dose adjustment needed
Ritonavir-Boosted Nirmatrelvir	TMR AUC ↑ 45%	No dose adjustment needed
Remdesivir	↔ expected	No dose adjustment needed
Herbal Products		
St. John's Wort	↓ TMR expected	Contraindicated
Hormonal Therapies		
Hormonal Contraceptives	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 (e.g., estradiol, 5-alpha reductase inhibitors, testosterone)	↑ estradiol possible	Use lowest effective dose for estrogen-containing regimens.
Menopausal Hormone Replacement Therapy (e.g., conjugated estrogens, drospirenone, estradiol, medroxyprogesterone, progesterone)	↑ estrogens, estradiol possible	Use lowest effective dose for estrogen-containing regimens.
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.

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
Narcotics and Treatment for Opioid Dependence		
Buprenorphine/Naloxone	Buprenorphine AUC ↑ 30% Norbuprenorphine (active metabolite) AUC ↑ 39%	No dose adjustment needed
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
ETR	TMR AUC ↓ 50% ↔ ETR	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 plus DRV/r	TMR C_{max} and AUC ↑ 34% to 53% ↔ DRV, RTV ETR AUC ↑ 28%	No dose adjustment needed
PIs		
ATV/c	↑ TMR expected ↔ 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

[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
↔ = less than 20% change in AUC

Key: ALT = alanine aminotransferase; ARV = antiretroviral; AST = aspartate aminotransferase; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; C_{max} = maximum plasma concentration; CAB = cabotegravir; CCR5 = C-C chemokine receptor type 5; CMV = cytomegalovirus; 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; gp120 = glycoprotein 120; HCV = hepatitis C virus; IBA = ibalizumab; IM = intramuscular; INSTI = integrase strand transfer inhibitor; LEN = lenacapavir; 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 fumarate; TMR = temsavir

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

Updated: September 12, 2024
Reviewed: September 12, 2024

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 judgment 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 herbal 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
Acid Reducers		
Antacids, H2 Receptor Antagonists, Proton Pump Inhibitors	↔ expected	No dose adjustment needed
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	Initiate tamsulosin at 0.4 mg/day. Monitor blood pressure.
Terazosin	↔ expected	No dose adjustment needed
Silodosin	↑ silodosin 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
Antibacterials—Antimycobacterials		
Bedaquiline	↑ bedaquiline expected	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	Daily and Weekly Dosing • ↓ LEN expected	Do not coadminister.
Antibacterials—Macrolides		
Azithromycin	↔ expected	No dose adjustment needed
Clarithromycin	↑ LEN possible	No dose adjustment needed
Erythromycin	↑ LEN possible	No dose adjustment needed
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.
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.
Desvenlafaxine	↔ expected	No dose adjustment needed
Duloxetine	↔ 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
Mirtazapine	↑ mirtazapine possible	No dose adjustment needed. Monitor for mirtazapine-related adverse events.
Nefazodone	↑ LEN possible	No dose adjustment needed
Selective Serotonin Reuptake Inhibitor (e.g., citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, vortioxetine)	↑ paroxetine possible ↔ citalopram, escitalopram, fluoxetine, fluvoxamine, sertraline, vortioxetine expected	Dose reduction may be necessary with paroxetine. No dose adjustment needed
Trazodone	↑ trazodone expected	Administer lowest dose of trazodone and monitor for CNS and CV adverse events.
Tricyclic Antidepressants (e.g., amitriptyline, doxepin, nortriptyline)	↔ expected	No dose adjustment needed
Venlafaxine	↔ expected	No dose adjustment needed
Antipsychotics		
Aripiprazole	↑ aripiprazole possible	No dose adjustment needed
Brexpiprazole	↑ brexpiprazole expected	If patient is a known CYP2D6 poor metabolizer, then administer one-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	Reduce dose of lumateperone to 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 Olanzapine/Samidorphan	↔ LEN olanzapine expected ↑ samidorphan possible	No dose adjustment needed
Other Antipsychotics (e.g., clozapine, risperidone, thioridazine)	↑ clozapine possible	No dose adjustment needed. Monitor for clozapine-related adverse events.
	↑ risperidone possible	No dose adjustment needed
	↑ thioridazine possible ↓ LEN possible	Do not coadminister.
Pimavanserin	↑ pimavanserin possible	No dose adjustment needed. Monitor ECG for QTc prolongation.

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
Pimozide	↑ pimozide expected	Contraindicated
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
Antimigraine		
Ergot Derivatives	↑ dihydroergotamine, ergotamine, and methylergonovine expected	Do not coadminister.
Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonists		
Atogepant	↑ atogepant expected	No dose adjustment needed
Rimegepant	↑ rimegepant expected	Avoid a second dose of rimegepant within 48 hours.
Ubrogepant	↑ ubrogepant expected	Avoid a second dose of ubrogepant within 24 hours.
Zavegepant	↔ expected	No dose adjustment needed
Serotonin 5-HT1B, 1D Receptor Agonist		
Almotriptan	↔ expected	No dose adjustment needed
Eletriptan	↑ eletriptan expected	No dose adjustment needed. Monitor for eletriptan-related adverse events.
Frovatriptan, Naratriptan, Rizatriptan, Sumatriptan Zolmitriptan	↔ expected	No dose adjustment needed
Antifungals		
Fluconazole	↑ LEN possible	No dose adjustment needed
Ibrexafungerp	↑ ibrexafungerp possible	No dose adjustment needed
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.
Artesunate	↔ expected	No dose adjustment needed
Atovaquone/Proguanil	↔ expected	No dose adjustment needed
Mefloquine	↑ mefloquine possible	Monitor for mefloquine-related adverse events, including QTc prolongation.

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
Antiplatelets		
Clopidogrel	↓ clopidogrel active metabolite possible	Consider alternative ARV or antiplatelet drug. If coadministered, monitor for clopidogrel-related adverse events.
Prasugrel	↔ 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
Antipneumocystis and Antitoxoplasmosis		
Atovaquone Oral suspension	↔ expected	No dose adjustment needed
Antiseizure		
Carbamazepine	↓ LEN expected	Contraindicated
Eslicarbazepine	↓ LEN expected	Do not coadminister.
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.
Phenobarbital	↓ LEN expected	Do not coadminister.
Phenytoin	↓ LEN expected	Contraindicated
Primidone	↓ LEN expected	Do not coadminister.
Valproic Acid	↔ expected	No dose adjustment needed
Antivirals—Hepatitis C		
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
Antivirals—Miscellaneous (e.g., for CMV, Mpox)		
Brincidofovir	↔ expected	No dose adjustment needed
Cidofovir	↔ expected	No dose adjustment needed
Maribavir	↔ expected	No dose adjustment needed
Tecovirimat	↓ LEN possible	No dose adjustment needed
Valganciclovir	↔ 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
Antivirals—SARS-CoV-2		
Molnupiravir	↔ expected	No dose adjustment needed
Ritonavir-Boosted Nirmatrelvir	↑ LEN possible	No dose adjustment needed
Remdesivir	↔ expected	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.
DOR	↑ DOR possible	No dose adjustment needed
RPV (IM or PO)	↑ RPV possible	No dose adjustment needed
PIs		
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
Beta-Agonists, Long-Acting Inhaled		
Arformoterol, Formoterol, Indacaterol, Olodaterol, Salmeterol	↔ 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
Cardiac Medications		
Antiarrhythmics		
Amiodarone	↑ amiodarone expected ↑ LEN possible	Do not coadminister.
Digoxin	↑ digoxin expected	Consider alternative ARV or antiarrhythmic. If coadministered, monitor digoxin therapeutic concentration.
Disopyramide	↑ disopyramide expected	Do not coadminister.
Dofetilide	↔ expected	No dose adjustment needed
Dronedarone	↑ dronedarone possible ↑ LEN possible	Consider alternative ARV or cardiac medication. If coadministered, monitor for dronedarone-related adverse events.
Flecainide	↔ expected	No dose adjustment needed
Lidocaine	↑ propafenone possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor for antiarrhythmic-related adverse events and monitor concentrations, if available.
Mexiletine	↔ expected	No dose adjustment needed
Propafenone	↑ propafenone possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor for antiarrhythmic-related adverse events and monitor concentrations, if available.
Quinidine	↑ quinidine expected	Do not coadminister.
Sotalol	↔ expected	No dose adjustment needed
Beta-Blockers		
Atenolol, Bisoprolol, Carvedilol, Labetalol, Metoprolol, Nebivolol, Timolol	↔ expected	No dose adjustment needed
Calcium Channel Blockers		
Amlodipine, Felodipine, Nifedipine	↑ amlodipine, felodipine expected ↑ nifedipine possible	Monitor and dose adjust according to clinical response and adverse events.
Diltiazem, Verapamil	↑ diltiazem possible ↔ verapamil expected	No dose adjustment needed
Cardiac – Other		
Bosentan	↓ 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
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.
Ivabradine	↑ ivabradine expected	Do not coadminister.
Mavacamten	↓ LEN possible ↑ mavacamten expected	Initiate mavacamten at the recommended starting dose of 5 mg daily in patients who are on stable therapy with LEN. Reduce dose of mavacamten by one level (i.e., 15 to 10 mg, 10 to 5 mg, or 5 to 2.5 mg) in patients who are on mavacamten treatment and intend to initiate LEN.
Ranolazine	↑ ranolazine expected	Limit ranolazine to 500 mg twice daily.
Corticosteroids		
Beclomethasone Inhaled or intranasal Ciclesonide Inhaled	↔ expected	No dose adjustment needed
Budesonide, Fluticasone, Mometasone Inhaled or intranasal	↑ glucocorticoids 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	↑ betamethasone possible ↓ LEN possible	Do not coadminister.
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

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
		>16 mg/day.
Betamethasone, Methylprednisolone, Triamcinolone 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		
Canagliflozin	↔ expected	No dose adjustment needed
Saxagliptin	↑ saxagliptin possible	No dose adjustment needed
Dapagliflozin/Saxagliptin	↑ saxagliptin possible	No dose adjustment needed
Herbal Products		
St. John's Wort	↓ LEN expected	Contraindicated
Hormonal Therapies—Contraceptives		
Injectable Contraceptives Depot MPA	↑ MPA possible	No dose adjustment needed
Oral Contraceptives (e.g., desogestrel, drospirenone, ethinyl estradiol, levonorgestrel, norgestimate)	↑ contraceptive exposures possible	No dose adjustment needed
Subdermal Implant Contraceptives (e.g., etonogestrel, levonorgestrel)	↑ contraceptive exposures possible	No dose adjustment needed
Transdermal Contraceptives (e.g., ethinyl estradiol/norelgestromin, ethinyl estradiol/levonorgestrel)	↑ contraceptive exposures possible	No dose adjustment needed
Vaginal Ring Contraceptives (e.g., etonogestrel/ethinyl estradiol, segesterone/ethinyl estradiol)	↑ contraceptive exposures possible	No dose adjustment needed
Emergency Contraceptives Levonorgestrel (oral)	↑ levonorgestrel possible	No dose adjustment needed
Hormonal Therapies—Gender Affirming and Menopause		
Estradiol	↔ expected	No dose adjustment needed
5-Alpha Reductase Inhibitors (e.g., dutasteride, finasteride)	↑ dutasteride and finasteride possible	No dose adjustment needed
Testosterone	↑ testosterone possible	No dose adjustment needed
Other Gender-Affirming Medications	↔ goserelin, leuprolide acetate expected	No dose adjustment needed
Menopausal Hormone Replacement Therapy (e.g., conjugated estrogens, drospirenone, estradiol, medroxyprogesterone, progesterone)	↑ estrogen and progesterone possible ↑ drospirenone 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
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		
Atorvastatin	↑ atorvastatin possible	No dose adjustment needed
Fluvastatin	↔ expected	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	Initiation of Methadone in Patients Taking LEN • Titrate methadone dose to desired effect and use the lowest feasible initial dose.

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
		Initiation of LEN in Patients Taking Methadone • Dose adjustment for methadone may be needed. Monitor for buprenorphine-related adverse events.
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	For Treatment of Erectile Dysfunction • For once-daily use: Consider maximum dose of 2.5 mg daily. If higher dose is needed, consider alternative PDE5 inhibitor. • For use as needed: Consider maximum dose of 10 mg every 72 hours. If higher dosing is needed, consider alternative PDE5 inhibitor. For Treatment of PAH • Do not coadminister. For Treatment of Benign Prostatic Hyperplasia • Consider maximum dose of 2.5 mg daily. Use caution and monitor for AEs if dose increases to 5 mg.
Vardenafil	↑ vardenafil expected	Vardenafil dose should not exceed 5 mg once every 24 hours.

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
Sedative/Hypnotics		
Benzodiazepines		
Alprazolam, Diazepam, Triazolam	↑ alprazolam expected	Consider lowest dose and monitor for benzodiazepine-related adverse events.
Clonazepam	↑ clonazepam possible	Use with caution and consider alternative benzodiazepines.
Lorazepam, Oxazepam, Temazepam	↔ expected	No dose adjustment needed
Midazolam (Oral), Triazolam	↑ midazolam AUC 259-308%	Use with caution and consider alternative benzodiazepine.
Orexin Receptor Antagonist		
Daridorexant, Lemborexant, Suvorexant	↑ daridorexant expected ↑ lemborexant expected ↑ suvorexant expected	Maximum recommended daridorexant dose is 25 mg. Do not coadminister with lemborexant. 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. Do not exceed 10 mg per night.
Other Sedatives		
Eszopiclone	↑ eszopiclone expected	Consider lowest dose and monitor for eszopiclone-related adverse events.
Zolpidem	↑ zolpidem possible	Consider initiating zolpidem at a low dose.
Miscellaneous Drugs		
Calcifediol	↑ calcifediol possible	No dose adjustment needed
Cisapride	↑ cisapride expected	Do not coadminister.
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).
Dronabinol	↔ expected	No dose adjustment needed
Eluxadoline	↔ 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
Finerenone	↑ finerenone expected	Monitor serum potassium at initiation and during therapy according to finerenone product labeling.
Flibanserin	↑ flibanserin expected	Contraindicated
Naloxegol	↑ naloxegol expected	Avoid use; if coadministration is necessary, decrease dosage of naloxegol and monitor for naloxegol-related adverse events.
Praziquantel	↑ praziquantel possible	Consider alternative antiretroviral. If coadministration is necessary, monitor for praziquantel-related adverse events.

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

Key: 3TC = lamivudine; ABC = abacavir; AE = adverse event; AUC = area under the curve; ARV = antiretroviral; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; CAB = cabotegravir; CD4 = CD4 T lymphocyte; CHF = congestive heart failure; CMV = cytomegalovirus; CNS = central nervous system; CV = cardiovascular; CYP = cytochrome P450; 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; MI = myocardial infarction; MPA = medroxyprogesterone acetate; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; 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

Updated: September 12, 2024
Reviewed: September 12, 2024

Note: Interactions associated with unboosted atazanavir (ATV), delavirdine (DLV), fosamprenavir (FPV), indinavir (IDV), lopinavir (LPV), nelfinavir (NFV), nevirapine (NVP), saquinavir (SQV), and tipranavir (TPV) are **not** included in this table. Please refer to the U.S. 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 (CAB) IM plus RPV IM is a two-drug co-packaged product. Therefore, RPV IM is not expected to be used with a protease inhibitor.

PIs		NNRTIs			
		DOR	EFV	ETR	RPV
ATV/c	PK Data	↑ DOR expected ↔ ATV expected	↔ EFV expected ↓ ATV possible ↓ COBI possible	↑ ETR 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.	No dose adjustment needed

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

PIs		NNRTIs			
		DOR	EFV	ETR	RPV
ATV/r	PK Data	↑ DOR expected ↔ ATV expected	↔ EFV expected (ATV 400 mg Plus RTV 100 mg) Once Daily • ATV concentrations similar to (ATV 300 mg plus RTV 100 mg) without EFV	(ATV 300 mg Plus RTV 100 mg) Once Daily • ETR AUC and C_{min} both ↑ ~30% • ↔ ATV AUC and C_{min}	↑ RPV PO possible ↔ ATV expected
	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	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%	↔ DRV expected ↑ RPV PO possible
	Dose	No dose adjustment needed	Do not coadminister.	Do not coadminister.	No dose adjustment needed

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

PIs		NNRTIs			
		DOR	EFV	ETR	RPV
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	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 have been established in a clinical trial.	No dose adjustment needed

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

Key: ART = antiretroviral therapy; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; C_{min} = minimum plasma concentration; COBI = cobicistat; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; EFV = efavirenz; ETR = etravirine; NNRTI = non-nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PO = oral; PK = pharmacokinetic; RPV = rilpivirine; RTV = ritonavir

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

Updated: September 12, 2024
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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 people with HIV for short-term use only (PO lead-in and to bridge if intramuscular [IM] administration is delayed).

CAB IM and rilpivirine (RPV) IM 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 PO non-nucleoside reverse transcriptase inhibitors (NNRTIs) or protease inhibitors (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}

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
	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.
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%	↑ 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 or DRV/r. In Patients Without INSTI Resistance • DTG 50 mg once daily with ETR (concurrently with ATV/r or DRV/r)	Do not coadminister.	RAL 400 mg twice daily Coadministration with RAL 1,200 mg once daily is not recommended.

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
			In Patients With Certain INSTI-Associated Resistance[a] or Clinically Suspected INSTI Resistance • DTG 50 mg twice daily with ETR (concurrently with ATV/r or DRV/r)		
RPV	PK Data	No data	With DTG 50 mg Once Daily • ↔ DTG AUC and C_{min} ↑ 22% • ↔ RPV PO AUC and C_{min} ↑ 21%	↑ 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/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 Cmin ↑ 38%
	Dose	No dose adjustment needed.	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
↔ = less than 20% change in AUC

Key: ARV = antiretroviral; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; C_{min} = minimum plasma concentration; 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; INSTI = integrase strand transfer inhibitor; NNRTI = non-nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PK = pharmacokinetic; PO = oral; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir

Appendix B, Table 1. Coformulated and Copackaged Antiretroviral Regimens

Updated: September 12, 2024
Reviewed: September 12, 2024

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 Appendix A in 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

Appendix B, Table 1. Coformulated and Copackaged Antiretroviral Regimens

Trade Name (Abbreviation)	ARV Drugs Included in the Regimen	Dosing Recommendation[a]
INSTI Plus One NNRTI		
Cabenuva (CAB IM and RPV IM)	Cabenuva 600-mg/900-mg Kit: • CAB 600-mg/3-mL vial and RPV 900-mg/3-mL vial Cabenuva 400-mg/600-mg Kit: • CAB 400-mg/2-mL vial and RPV 600-mg/2-mL vial	Optional Lead-In With Oral CAB and RPV • CAB 30 mg PO 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 for 1 dose and RPV 900 mg/3 mL IM for 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
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
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

Appendix B, Table 1. Coformulated and Copackaged Antiretroviral Regimens

Trade Name (Abbreviation)	ARV Drugs Included in the Regimen	Dosing Recommendation[a]
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
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

[a] For dose adjustments in people 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 = intramuscularly; 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: September 12, 2024

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 Appendix A in 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 people 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

Updated: May 26, 2023
Reviewed: September 12, 2024

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 Appendix A in 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 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 people with hepatic insufficiency (see Appendix B, Table 12).	1.5 hours/12–26 hours	People who test positive for HLA-B*5701 are at the highest risk of experiencing HSRs. HLA screening should be done before initiating ABC. For people 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,

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]
					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) • Truvada (TDF/FTC) STRs That Contain FTC[d] • Atripla (EFV/TDF/FTC) • Biktarvy (BIC/TAF/FTC) • Complera (RPV/TDF/FTC) • Genvoya (EVG/c/TAF/FTC) • Odefsey (RPV/TAF/FTC) • Stribild (EVG/c/TDF/FTC) • Symtuza (DRV/c/TAF/FTC)	Emtriva *Capsule* • FTC 200 mg PO once daily *Oral Solution* • FTC 240 mg (24 mL) PO once daily See Appendix B, Tables 1 and 2 for dosing information for FDC tablets that contain FTC.	86% of FTC dose is excreted renally. See Appendix B, Table 12 for dosing recommendations in people with renal insufficiency.	10 hours/ >20 hours	Minimal toxicity Hyperpigmentation/skin discoloration Severe acute exacerbation of hepatitis may occur in people with HBV/HIV coinfection who discontinue 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	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 people with renal insufficiency.	5–7 hours/18–22 hours	Minimal toxicity Severe acute exacerbation of hepatitis may occur in people 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]
	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)				
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 people 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 people with HBV/HIV coinfection who discontinue TAF. Diarrhea, nausea, headache Greater weight increase has been reported with TAF than with 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]
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) • Stribild (EVG/c/TDF/FTC) • Symfi (EFV 600 mg/TDF/3TC) • Symfi Lo (EFV 400 mg/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.** See Appendix B, Tables 1 and 2 for dosing information for FDC tablets that contain TDF.	Renal excretion is the primary route of elimination. See Appendix B, Table 12 for dose recommendations in people 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 people with HBV/HIV coinfection who discontinue TDF.

[a] For dose adjustments in people 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

Updated: September 12, 2024
Reviewed: September 12, 2024

The following table includes dose recommendations for U.S. Food and Drug Administration (FDA)–approved non-nucleoside reverse transcriptase inhibitor (NNRTI) 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 Appendix A in the Pediatric Antiretroviral Guidelines. The older NNRTIs delavirdine (DLV) and nevirapine (NVP) are **not** listed in this table; DLV has been discontinued and NVP is no longer commonly used in clinical practice in the United States.

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 STRs That Contain DOR[c] • Delstrigo (DOR/TDF/3TC)	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 on an empty stomach, preferably at or before bedtime 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.

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]
Etravirine (ETR) *Intelence*	Intelence • 100-mg and 200-mg tablets	Intelence • ETR 200 mg PO twice daily following a meal.	CYP3A4, 2C9, and 2C19 substrate CYP3A4 inducer CYP2C9 and 2C19 inhibitor	41 hours	Rash, including Stevens-Johnson syndrome[d] HSRs, characterized by rash, constitutional findings, and sometimes organ dysfunction (including hepatic failure), have been reported. Nausea
Rilpivirine (RPV) *Edurant*	Edurant • 25-mg tablet 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 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] Depressive disorders, insomnia, headache Hepatotoxicity QT interval prolongation IM Formulation Only • Injection site reactions (pain, induration, swelling, nodules) • Rare postinjection 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 people 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 1 for information about these formulations.

[d] Rare cases of Stevens-Johnson syndrome have been reported with the use of most NNRTIs.

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

[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 people 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 people. 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; PO = orally; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Appendix B, Table 5. Characteristics of Protease Inhibitors

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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 Appendix A in the Pediatric Antiretroviral Guidelines. The older protease inhibitors indinavir (IDV) and saquinavir (SQV) have been discontinued in the United States; fosamprenavir (FPV), lopinavir/ritonavir (LPV/r), 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 the Archived Guidelines webpage on the Clinicalinfo website) or to the FDA 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 People Without Prior ARV Treatment* • (ATV 300 mg plus RTV 100 mg) PO once daily with food; *or* • ATV 400 mg PO once daily with food. *With TDF or in ARV-Experienced People* • (ATV 300 mg plus RTV 100 mg) PO once daily with food. • Unboosted ATV is not recommended. *With EFV in People Without Prior ARV Treatment* • (ATV 400 mg plus RTV 100 mg) PO once daily with food. Evotaz • One tablet PO once daily with food.	ATV • CYP3A4 inhibitor and substrate • Weak CYP2C8 inhibitor • UGT1A1 inhibitor COBI • CYP3A inhibitor and substrate • CYP2D6 inhibitor Dose adjustment is recommended in people 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 Lipodystrophy An increase in serum creatinine may occur when ATV is administered with COBI.

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 people 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 people who also are receiving H2 antagonists and PPIs, refer to Table 24a.			PR interval prolongation: First-degree symptomatic AV block has been reported. Use with caution in people who have underlying conduction defects or who are on concomitant medications that can cause PR prolongation.
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 People Without Prior ARV Treatment or ARV-Experienced Treatment With No DRV Mutations* • (DRV 800 mg plus RTV 100 mg) PO once daily with food. *In ARV-Experienced People With One or More DRV Resistance Mutations* • (DRV 600 mg plus RTV 100 mg) PO twice daily with food. Unboosted DRV **is not recommended**. Prezcobix • One tablet PO once daily with food. • **Not recommended** for people with one or more DRV resistance-associated mutations. • Coadministering Prezcobix and TDF **is not recommended** for people 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 Lipodystrophy 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.			
Ritonavir (RTV) *Norvir* Note: Generic is available. RTV was initially developed as a PI for HIV treatment but is now primarily used at a lower dose of 100 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 100–200 mg PO per day in one or two divided doses (refer to other PIs for specific dosing recommendations) 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 Dysgeusia Hyperglycemia Fat maldistribution

[a] For dose adjustments in people 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/r = lopinavir/ritonavir; 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: September 12, 2024
Reviewed: September 12, 2024

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 AppendixA in 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	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	IM formulation only: Injection site reactions (e.g., pain, induration, swelling, nodules) The following AEs were reported when CAB was administered in combination with RPV: Headache Nausea

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]
	• Must be obtained from manufacturer for oral lead-in and oral bridging during administration of Cabenuva (CAB IM/RPV IM)				Abnormal dreams Anxiety Insomnia Depressive disorders Hepatotoxicity
Dolutegravir (DTG) *Tivicay*	Tivicay • 50-mg tablet STRs That Contain DTG[c] • Dovato (DTG/3TC) • Juluca (DTG/RPV) • Triumeq (DTG/ABC/3TC)	In People Without Prior ARV Treatment or ARV-Experienced People Who Had Never Received INSTIs • DTG 50 mg PO once daily In People Without Prior ARV Treatment or ARV-Experienced People Who Had Never Received INSTIs When Coadministered With EFV, FPV/r, TPV/r, or Rifampin • DTG 50 PO mg twice daily In INSTI-Experienced People 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 Depressive disorders and suicidal ideation (rare; usually occurs in people with preexisting psychiatric conditions) Weight gain Hepatotoxicity HSRs, including rash, constitutional symptoms, and organ dysfunction (including liver injury), have been reported.

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]
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 people 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 people with preexisting psychiatric conditions)
Raltegravir (RAL) *Isentress* *Isentress HD*	Isentress • 400-mg tablet • 100-mg single-use packet for oral suspension Isentress HD • 600-mg tablet	Isentress • 400 mg PO twice daily *With Rifampin* • 800 mg PO twice daily Isentress HD *In People Without Prior ARV Treatment or ARV-Experienced People 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

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]
					Weight gain Insomnia Depression and suicidal ideation (rare; usually occurs in people with preexisting psychiatric conditions)

[a] For dose adjustments in people 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; AE = adverse event; 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: September 12, 2024

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 Appendix A in 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 all people Increased incidence of bacterial pneumonia HSR occurs in <1% of people. Symptoms may include rash, fever, nausea, vomiting, chills, rigors, hypotension, or elevated serum transaminases. Rechallenge 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: September 12, 2024

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 Appendix A in 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 people with severe renal insufficiency

[a] For dose adjustments in people 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: September 12, 2024

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

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Serum Half-Life	Elimination/ Metabolic Pathway	Adverse Events[a]
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 people who are receiving IBA.	~64 hours	Not well defined	Diarrhea Dizziness Nausea Rash HSRs, including anaphylaxis and infusion-related reactions, have been reported.

[a] Also see Table 20.

Key: HSR = hypersensitivity reaction; IBA = ibalizumab; IV = intravenous

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

Updated: May 26, 2023
Reviewed: September 12, 2024

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

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Serum Half-Life	Elimination/ Metabolic Pathway	Adverse Events[a]
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 four times the recommended dose. Use with caution in people with preexisting heart disease, QTc prolongation, or concomitant use of medications that may prolong QTc interval.

[a] also see Table 20.

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

Appendix B, Table 11. Characteristics of the Capsid Inhibitor

Updated: September 12, 2024
Reviewed: September 12, 2024

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

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Serum Half-Life	Elimination/ Metabolic Pathway	Adverse Events[a]
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) Note: Each SQ dose requires two injections.	PO: 10–12 days SQ: 8–12 weeks	Substrate of P-glycoprotein, CYP3A (minor), UGT1A1 (minor) CYP3A4 inhibitor (moderate)	Injection site reactions, including nodules and induration Nausea, diarrhea, headache

[a] Also see Table 20.

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: September 12, 2024
Reviewed: September 12, 2024

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 Appendix A in the Pediatric Antiretroviral Guidelines.

The older antiretroviral drugs fosamprenavir (FPV), lopinavir/ritonavir (LPV/r) , nelfinavir (NFV), nevirapine (NVP), 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
Recommendations for FDCs based on CrCl level are outlined in the table below.			
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
Abacavir/Lamivudine (ABC/3TC) *Epzicom*	One tablet PO once daily	Not FDA recommended if CrCl <30 mL/min due to the 3TC component. Note: There is insufficient evidence to recommend for or against the use of full-dose 3TC in people with CrCl <30 mL/min. Some Panel members use full-dose 3TC to allow people to remain on the FDC product. See the 3TC entry for more information.	*Child-Pugh Class A:* People with mild hepatic impairment require a dose reduction of ABC. Use the individual drugs instead of the FDC tablet in these people. *Child-Pugh Class B or C:* Contraindicated due to the ABC component

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 colspan="3">Dosing in Adults With Renal Insufficiency</th><th>Dosing in Adults With Hepatic Impairment</th></tr>
<tr><td rowspan="5">Emtricitabine
(FTC)
Emtriva</td><td rowspan="5">FTC 200-mg oral capsule once daily
or
FTC 240-mg (24-mL) oral solution once daily

Note: There is insufficient evidence to recommend for or against the use of full-dose, daily FTC in people with CrCl <30 mL/min who are not on HD. To allow people to remain on certain TAF-containing FDC products, some Panel members use full-dose, daily FTC in people with CrCl 15–29 mL/min who are not on HD.</td><td colspan="3">Dose by Formulation</td><td rowspan="5">No dose recommendation.</td></tr>
<tr><td>CrCl (mL/min)</td><td>Capsule</td><td>Solution</td></tr>
<tr><td>30–49[b]</td><td colspan="2">No dose adjustment necessary.</td></tr>
<tr><td>15–29
(see Note)</td><td>200 mg every 72 hours</td><td>80 mg every 24 hours</td></tr>
<tr><td><15 (not on HD)
(see Note)</td><td>200 mg every 96 hours</td><td>60 mg every 24 hours</td></tr>
<tr><td rowspan="4">Lamivudine[c]
(3TC)
Epivir</td><td rowspan="4">3TC 300 mg PO once daily
or
3TC 150 mg PO twice daily

Note: PK and safety data are limited on the use of 3TC doses higher than those recommended by the FDA in people with CrCl <30 mL/min. Clinicians may consider using the nearest available tablet strength (100 mg or 150 mg), as outlined in the “Alternative Dose” column (BIII) (see rationale[d]). There is insufficient evidence to recommend for or against the use of full-dose 3TC in people with CrCl <30 mL/min. Some Panel members use full-dose 3TC to allow people to remain on certain ABC and/or DTG-containing FDC products.</td><td>CrCl (mL/min)</td><td>Epivir Label Dose</td><td>Alternative Dose[d]</td><td rowspan="4">No dose adjustment necessary</td></tr>
<tr><td>15–29
(see Note)</td><td>1 × 150 mg, then 100 mg every 24 hours</td><td>100–150 mg every 24 hours</td></tr>
<tr><td>5–14
(see Note)</td><td>1 × 150 mg, then 50 mg every 24 hours</td><td>100–150 mg every 24 hours</td></tr>
<tr><td><5 or on HD
(see Note)</td><td>1 × 50 mg, then 25 mg every 24 hours</td><td>100–150 mg every 24 hours</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 A:* No dose adjustment *Child-Pugh Class B or C:* Not recommended
		<15 (not on HD)	Not recommended	
		On HD	No dose adjustment necessary. On HD days, administer after dialysis.	
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
		15–29	Not recommended Note: There is insufficient evidence to recommend for or against the use of full-dose, daily FTC in people with CrCl <30 mL/min. To allow people to remain on the FDC product, some Panel members use full-dose FTC in people with CrCl 15–29 mL/min.	
		<15 (not on HD)	Not recommended	
		On HD	No dose adjustment necessary. On HD days, administer after dialysis.	
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 (not on HD)	No recommendation	
		On HD	300 mg every 7 days (administer after completion of HD)	

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 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	FDC of TDF/FTC 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	FDC of TDF/3TC not recommended	
NNRTIs				
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	FDC of DOR/TDF/3TC not recommended if CrCl <50 mL/min or on HD		*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 people with hepatic impairment.
Efavirenz/Tenofovir Disoproxil Fumarate/ Emtricitabine (EFV/TDF/FTC) *Atripla*	One tablet PO once daily on an empty stomach, preferably at bedtime	FDC of EFV/TDF/FTC not recommended if CrCl <50 mL/min or if on HD		No dose recommendation; use with caution in people with hepatic impairment.

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
Efavirenz 600 mg/ Tenofovir Disoproxil Fumarate/ Lamivudine (EFV/TDF/3TC) *Symfi*	One tablet PO once daily on an empty stomach, preferably at bedtime	FDC of EFV/TDF/3TC not recommended if CrCl <50 mL/min or if on HD	Not recommended for people with moderate or severe hepatic impairment. Use with caution in people 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	FDC of EFV/TDF/3TC not recommended if CrCl <50 mL/min or if on HD	Not recommended for people with moderate or severe hepatic impairment. Use with caution in people 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
Rilpivirine (RPV PO) *Edurant*	RPV 25 mg PO once daily with food	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
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-Months 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 people 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 with food	In People With CrCl 15–29 mL/min • Not recommended • Note: There is insufficient evidence to recommend for or against the use of full-dose, daily FTC in people with CrCl <30 mL/min. To allow people to remain on the FDC product, some Panel members use full-dose, daily FTC in people with CrCl 15–29 mL/min. In People With CrCl <15 mL/min (not on HD) • Not recommended In People on Chronic HD • No dose adjustment necessary. On HD days, administer after dialysis.	*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 with food	FDC of RPV/TDF/FTC not recommended if CrCl <50 mL/min or on HD	*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 people 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 with food *or* (ATV 300 mg plus RTV 100 mg) PO once daily with food	In People Without Prior ARV Treatment on HD • (ATV 300 mg plus RTV 100 mg) once daily with food. In ARV-Experienced People 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 people without prior ARV treatent *Child-Pugh Class C:* Not recommended RTV boosting is not recommended in people with hepatic impairment.
Atazanavir/Cobicistat (ATV/c) *Evotaz*	One tablet PO once daily with food	If Used With TDF • Not recommended if CrCl <70 mL/min	Not recommended in people with hepatic impairmen.

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 (DRV) *Prezista*	In People Without Prior ARV Treatment or ARV-Experienced Treatment With No DRV Mutations • (DRV 800 mg plus RTV 100 mg) PO once daily with food. In ARV-Experienced People With at Least One DRV Resistance Mutation • (DRV 600 mg plus RTV 100 mg) PO twice daily with food.	No dose adjustment necessary	*In People With Mild-to-Moderate Hepatic Impairment:* No dose adjustment *In People With Severe Hepatic Impairment:* Not recommended
Darunavir/Cobicistat (DRV/c) *Prezcobix*	One tablet PO once daily with food	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 with food	In People With CrCl 15–29 mL/min • Not recommended • Note: There is insufficient evidence to recommend for or against the use of full-dose, daily FTC in people with CrCl <30 mL/min. To allow people to remain on the FDC product, some Panel members use full-dose, daily FTC in people with CrCl 15–29 mL/min. In People With CrCl <15 mL/min (not on HD) • Not recommended In People on Chronic HD • No dose adjustment necessary. On HD days, administer after dialysis.	Not recommended for people with severe hepatic impairment

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
Ritonavir (RTV) *Norvir*	As a PI-Boosting Agent • RTV 100–400 mg PO per day with food.	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 People With CrCl 15–29 mL/min • Not recommended • Note: There is insufficient evidence to recommend for or against the use of full-dose, daily FTC in people with CrCl <30 mL/min. To allow people to remain on the FDC product, some Panel members use full-dose, daily FTC in people with CrCl 15–29 mL/min. In People With CrCl <15 mL/min (not on HD) • Not recommended In People on Chronic HD • No dose adjustment necessary. On HD days, administer after dialysis.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* Not recommended
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

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 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 people 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
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

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/Abacavir/ Lamivudine (DTG/ABC/3TC) *Triumeq*	One tablet PO once daily	Not FDA recommended if CrCl <30 mL/min due to the 3TC component Note: There is insufficient evidence to recommend for or against the use of full-dose 3TC in people with CrCl <30 mL/min. Some Panel members use full-dose 3TC to allow people to remain on the FDC product.[d]	*Child-Pugh Class A:* People with mild hepatic impairment require a dose reduction of ABC. Use the individual drugs instead of the FDC tablet in these people. *Child-Pugh Class B or C:* Contraindicated due to the ABC component
Dolutegravir/Lamivudine (DTG/3TC) *Dovato*	One tablet PO once daily	Not FDA recommended if CrCl <30 mL/min due to 3TC component Note: There is insufficient evidence to recommend for or against the use of full-dose 3TC in people with CrCl <30 mL/min. Some Panel members use full-dose 3TC to allow people to remain on the FDC product.[d]	*Child-Pugh Class C:* Not recommended
Dolutegravir/Rilpivirine (DTG/RPV) *Juluca*	One tablet PO once daily with food	No dose adjustment necessary In people 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 with food	In People With CrCl 15–29 mL/min • Not recommended • Note: There is insufficient evidence to recommend for or against the use of full-dose, daily FTC in people with CrCl <30 mL/min. To allow people to remain on the FDC product, some Panel members use full-dose, daily FTC in people with CrCl 15–29 mL/min. In People With CrCl <15 mL/min (not on HD) • Not recommended In People on Chronic HD • No dose adjustment necessary. On HD days, administer after dialysis.	*In People With Mild-to-Moderate Hepatic Insufficiency:* No dose adjustment necessary *In People 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
Elvitegravir/Cobicistat/ Tenofovir Disoproxil Fumarate/Emtricitabine (EVG/c/TDF/FTC) *Stribild*	One tablet PO once daily with food	EVG/c/TDF/FTC **should not be initiated** in people with CrCl <70 mL/min. Discontinue EVG/c/TDF/FTC if CrCl declines to <50 mL/min while on therapy.	*In People With Mild-to-Moderate Hepatic Insufficiency:* No dose adjustment necessary *In People With Severe Hepatic Insufficiency:* **Not recommended**
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 People With Mild-to-Moderate Hepatic Insufficiency:* No dose adjustment necessary *In People 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 People With CrCl <30 mL/min or People 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 people with hepatic impairment.

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
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			
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 FTC (Emtriva) recommends adjusted doses for people with CrCl 30–49 mL/min and people on hemodialysis. However, the prescribing information for several FDC products that contain FTC (including Descovy, Biktarvy, Genvoya, and Odefsey) recommends that the standard dose (FTC 200 mg) can be given once daily in these people. The recommendations in this table incorporates the dosing guidance from the FDC products.

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

[c] The prescribing information for 3TC (Epivir) recommends dosage adjustment from 300 mg once daily to 150 mg once daily for people with CrCl 30–49 mL/min. However, the prescribing information for several FDC products that contain 3TC (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.

[d] Use of 3TC doses higher than those recommended by the FDA for people with CrCl <30 mL/min has been reported in clinical practice [1-4] and endorsed in the Guidelines for Chronic Kidney Disease in People With HIV for many years [5]; limited published literature has supported the safety of this practice [2,3]. 3TC has a wide therapeutic index with no established correlation between elevated concentrations and AEs. Serious AEs, such as lactic acidosis and severe hematologic toxicities, have been reported in rare cases; however, these effects typically occurred when 3TC was used in combination with older NRTIs (such as didanosine, stavudine, zidovudine). Clinicians may consider using the nearest available tablet strength (100 mg or 150 mg) to avoid the need for 3TC oral solution, thereby simplifying ARV regimens and facilitating adherence (BIII). See the Alternative Dose column in 3TC table entry. There is insufficient evidence to recommend for or against the use of full-dose 3TC in people with CrCl <30 mL/min. Some Panel members use full-dose 3TC to allow people to remain on certain FDC products.

Key: 3TC = lamivudine; ABC = abacavir; AE = adverse effect; 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; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PK: pharmacokinetic; PI = protease inhibitor; PO = orally; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQ = subcutaneous; T-20 = enfuvirtide; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

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 people 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.