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

Updated: September 24, 2026
Reviewed: September 24, 2026

This table guides clinicians in choosing an initial antiretroviral (ARV) regimen according to various individual and regimen characteristics and specific clinical scenarios. ARV drugs/regimens that are listed as *Recommended Initial Regimens for Most People With HIV* or *Initial Antiretroviral Regimens for Certain Clinical Scenarios* are included in this table. 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 Advantages and Disadvantages of Antiretroviral Components for additional information regarding the advantages and disadvantages of particular ARV medications recommended to be used as part of initial therapy.

Individual 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	**Do not use** RPV-based regimens.	Higher rates of virologic failure have been observed in those with high pre-treatment HIV RNA levels.
	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** • BIC/TAF/FTC, *or* • DTG plus (TAF or TDF)[a] plus (3TC or FTC) 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 increased risk of treatment failure with DTG resistance.

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

Individual or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
	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, Use:** • (DRV/r or DRV/c) plus (TAF or TDF)[a] plus (3TC or FTC) **If No INSTI Resistance Is Identified, Use:** • BIC/TAF/FTC, *or* • DTG plus (TAF or TDF)[a] plus (3TC or FTC), *or* • DTG/3TC	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.
	No prior exposure to CAB-LA for PrEP *and* rapid ART initiation is desired (i.e., before drug resistance results are available)	**Use** • BIC/TAF/FTC, *or* • 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.**
	Prior exposure to INSTI-based PEP *or* suspected acquisition from someone with virologic failure on 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)	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, and because selection of INSTI-resistant virus is likely to be uncommon in the setting of INSTI-based PEP, an INSTI-based regimen can be started, pending the results of the INSTI genotype.

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

Individual or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
ART-Specific Characteristics	A one-pill, once-daily regimen is desired.	**STR Options as *Recommended Initial Regimens For Most People With HIV*:** • BIC/TAF/FTC • DTG/3TC • DRV/c/TAF/FTC (if history of CAB-LA use as PrEP without INSTI genotype results) **STR Options as *Initial ARV Regimens For Certain Clinical Scenarios*:** • DOR/TDF/3TC • DTG/ABC/3TC • RPV/TAF/FTC	**Do not use** DTG/ABC/3TC if the person is HLA-B*5701 positive. **Do not use** DTG/ABC/3TC or DTG/3TC in the setting of HBV coinfection without another potent, high barrier HBV agent (i.e., entecavir). **Do not use** RPV/TAF/FTC if HIV RNA is >100,000 copies/mL and/or CD4 count is <200 cells/mm^3.
	Food effects	BIC-, DOR-, or DTG-based regimens can be taken without regard to food.	Oral bioavailability of these regimens is not significantly affected by food.
		DRV/r- or DRV/c-based regimens and RPV/TAF/FTC should be taken with food.	Food improves absorption of these regimens.
Presence of Other Conditions	Chronic kidney disease	**Avoid** TDF, if possible, for CrCl <60 mL/min **Avoid** TAF for CrCl <30 mL/min (unless on HD) Refer to Appendix B for specific ARV dosing recommendations in people with renal impairment. For people with progressively declining renal function, consider avoiding all TFV-containing (TAF or TDF) regimens.	TDF has been associated with proximal renal tubulopathy. Higher rates of renal dysfunction have been reported in people using TDF in conjunction with RTV- or COBI- containing regimens. TAF has less impact on renal dysfunction than TDF. If a TDF- or TAF-based regimen cannot be used in the setting of HBV coinfection or unknown HBV status, use entecavir (see HBV/HIV Coinfection).

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

Individual or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
	Liver disease with cirrhosis	Some ARVs are contraindicated or may require dosage modification in people with Child-Pugh class B or C disease.	Refer to Appendix B for specific dosing recommendations. People 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.	See Weight Gain in People With Treated HIV for more information.
	Osteoporosis	**Avoid TDF,** if possible.[a]	TDF is associated with decreases in BMD, along with renal tubulopathy, urine phosphate wasting, and resultant osteomalacia, especially with RTV- or COBI-boosted regimens. TAF[a] and ABC are associated with smaller declines in BMD than TDF.
	Psychiatric illnesses	**Consider avoiding** RPV-based regimens. People 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.	RPV can exacerbate psychiatric symptoms and may be associated with suicidality. Some INSTIs have been associated with adverse neuropsychiatric effects in some retrospective cohort studies and case series. Refer to the Liverpool HIV Drug Interaction Checker for dosing recommendations when drugs used for psychiatric illnesses are used with certain ARVs.

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

Individual or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
	Cardiac QTc interval prolongation	**Consider avoiding** RPV-based regimens if the person is taking other medications with known risk of Torsades de Pointes or in people 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.	Evidence increasingly supports a relationship between ABC and major CV events.
	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.
	History of poor adherence to non-ARV medications or inconsistent engagement in care	Consider using regimens with a high genetic barrier to resistance, such as BIC, DTG, or a boosted PI.	In people with inconsistent adherence, DRMs are less likely to emerge if they are on regimens with a high genetic barrier to resistance.
	Pregnancy	Refer to the Perinatal Guidelines for further guidance on ARV use during pregnancy.	
Presence of Coinfections	HBV infection	**Avoid regimens** without TFV. **If TDF and TAF Are Contraindicated** • Entecavir should be added to a fully suppressive ARV regimen (see HBV/HIV Coinfection).	TDF, TAF, FTC, and 3TC are active against both HIV and HBV. However, 3TC and FTC are insufficient for HBV treatment when used alone due to the emergence of resistance.
	HCV treatment required	Refer to recommendations in HCV/HIV Coinfection, with special attention to potential interactions between ARV drugs and HCV drugs.	

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

Individual or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
	Concomitant use with rifamycin antibiotics (e.g., rifabutin, rifampin, and rifapentine)	Recommended regimens may require dose adjustment. See the drug–drug interaction tables (see the Liverpool HIV Drug Interaction Checker).	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; COBI = cobicistat; CrCl = creatinine clearance; CV = cardiovascular; CYP = cytochrome P450; DOR = doravirine; DRM = drug resistance mutation; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; FTC = emtricitabine; HBV = hepatitis B virus; HCV = hepatitis C virus; HD = hemodialysis; 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