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

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
Pre-ART Characteristics	CD4 count <200 cells/mm^3	Do Not Use the Following Regimens: • RPV-based regimens • DRV/r plus RAL	A higher rate of virologic failure has been observed in those with low pre-treatment CD4 counts.
	HIV RNA >100,000 copies/mL (also see next row if HIV RNA >500,000 copies/mL)	Do Not Use the Following Regimens: • RPV-based regimens • ABC/3TC with EFV or ATV/r • DRV/r plus RAL	Higher rates of virologic failure have been observed in those with high pre-treatment HIV RNA levels.
	HIV RNA >500,000 copies/mL	Do Not Use the Following Regimens: • RPV-based regimens • ABC/3TC with EFV or ATV/r • DRV/r plus RAL • DTG/3TC	For DTG/3TC, limited data are available in patients with viral loads above this threshold.
	HLA-B*5701 positive or result unknown	Do not use ABC-containing regimens.	ABC hypersensitivity, a potentially fatal reaction, is highly associated with the presence of the HLA-B*5701 allele.
	Prior exposure to CAB-LA PrEP.	Avoid INSTI-based regimens, unless an INSTI genotype shows no resistance mutations.	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

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		Recommended Regimen Pending INSTI Genotype Results • (DRV/r or DRV/c) plus (TAF or TDF)[a] plus (3TC or FTC)	infection and may select for resistant virus.
	An ARV regimen should be started before HIV drug resistance results are available (e.g., in a person with acute HIV) or when ART is being initiated rapidly.	Avoid NNRTI-based regimens and DTG/3TC. Avoid ABC. Recommended ARV Regimens in Persons Without Exposure to CAB-LA PrEP • BIC/TAF/FTC • DTG plus (TAF or TDF)[a] plus (3TC or FTC) • (DRV/r or DRV/c) plus (TAF or TDF)[a] plus (3TC or FTC) Recommended ARV Regimen in Persons on CAB-LA PrEP Prior to HIV Acquisition • (DRV/r or DRV/c) plus (TAF or TDF)[a] plus (3TC or FTC)	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. Transmitted resistance to DRV, BIC, and DTG is rare, and these drugs have high barriers to resistance. Mutations conferring resistance to INSTIs have been seen in association with CAB-LA PrEP. CAB-LA has a very long half-life, and drug exposure may persist at levels suboptimal to prevent infection and may select for resistant virus.
ART-Specific Characteristics	A one-pill, once-daily regimen is desired.	STR Options as Initial ART Include the Following: • BIC/TAF/FTC • DOR/TDF/3TC • DRV/c/TAF/FTC • DTG/ABC/3TC • DTG/3TC • EFV/TDF/FTC • EFV/TDF/3TC • EVG/c/TAF/FTC • EVG/c/TDF/FTC • RPV/TAF/FTC • RPV/TDF/FTC	Do not use DTG/ABC/3TC if the patient is HLA-B*5701 positive. DTG/3TC is not recommended if HIV RNA is >500,000 copies/mL. Do not use DTG/ABC/3TC or DTG/3TC in the setting of HBV coinfection or unknown HBV status. Do not use RPV-based regimens if HIV RNA is >100,000 copies/mL and CD4 count is <200 cells/mm^3. See Appendix B, Table 11 for ARV dose recommendations in the setting of renal impairment.

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	Food effects	Regimens That Can Be Taken Without Regard to Food • BIC-, DOR-, DTG-, or RAL-based regimens	Oral bioavailability of these regimens is not significantly affected by food.
		Regimens That Should Be Taken With Food • ATV/r- or ATV/c-based regimens • DRV/r- or DRV/c-based regimens • EVG/c/TAF/FTC[a] • EVG/c/TDF/FTC[a] • RPV-based regimens	Food improves absorption of these regimens. RPV-containing regimens should be taken with ≥390 calories of food.
		Regimens That Should Be Taken on an Empty Stomach • EFV-based regimens	Food increases EFV absorption and may increase CNS side effects.
Presence of Other Conditions	Chronic kidney disease (defined as CrCl <60 mL/min)	In general, avoid TDF. ABC may be used if patient is HLA-B*5701 negative. If HIV RNA is >100,000 copies/mL, do not use ABC/3TC plus EFV or ATV/r. TAF may be used if CrCl >30 mL/min or if the patient is on chronic hemodialysis (studied only with EVG/c/TAF/FTC). Consider avoiding ATV. ART Options When ABC, TAF, or TDF Cannot Be Used (For patients with HBV coinfection, consult Hepatitis B Virus/HIV Coinfection for HBV treatment options.) • DTG/3TC (if HIV RNA <500,000 copies/mL) • DRV/r plus 3TC	TDF has been associated with proximal renal tubulopathy. Higher rates of renal dysfunction have been reported in patients using TDF in conjunction with RTV-containing regimens. An adjusted dose of TDF can be used in patients with ESRD or in those who are on hemodialysis. Refer to Appendix B, Table 11 for specific dosing recommendations. TAF has less impact on renal function and lower rates of proteinuria than TDF. ATV has been associated with chronic kidney disease in some observational studies. ABC has not been associated with renal dysfunction.

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		• DRV/r plus RAL (if CD4 count >200 cells/mm^3 and HIV RNA <100,000 copies/mL)	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 11 for specific dosing recommendations. Patients with cirrhosis should be carefully evaluated by an expert in advanced liver disease.
	Concern for excess weight gain	For many people with HIV, gaining weight after starting ART is part of a "return to health." However, some ARV regimens are associated with greater weight gain than others, suggesting that particular drugs may contribute to weight gain.	Initiation of INSTI-containing regimens, particularly BIC and DTG, has been associated with greater weight gain than NNRTI-containing or boosted PI-regimens. Greater weight gain has been observed with initiation of TAF than TDF or with a switch from TDF to TAF. ARV-associated weight gain appears to disproportionately affect women and Black and Hispanic people.
	Osteoporosis	Avoid TDF.[a] ABC may be used if the patient is HLA-B*5701 negative. If HIV RNA is >100,000 copies/mL, do not use ABC/3TC plus (EFV or ATV/r).	TDF is associated with decreases in BMD along with renal tubulopathy, urine phosphate wasting, and resultant osteomalacia. TAF[a] and ABC are associated with smaller declines in BMD than TDF.
	Psychiatric illnesses	Consider avoiding EFV- and RPV-based regimens. Patients on INSTI-based regimens who have preexisting psychiatric conditions should be closely monitored.	EFV and RPV can exacerbate psychiatric symptoms and may be associated with suicidality. INSTIs have been associated with adverse neuropsychiatric effects in some retrospective cohort studies and case series.

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		Some ARVs are contraindicated, and some psychiatric medications need dose adjustments when coadministered with certain ARVs.	See the drug–drug interaction tables (Tables 24a, 24b, and 24d) for dosing recommendations when drugs used for psychiatric illnesses are used with certain ARVs.
	HIV-associated dementia	Avoid EFV-based regimens if possible.	The beneficial effects of ART on HIV-associated dementia symptoms may be confounded by EFV-related neuropsychiatric effects.
	Medication-assisted treatment for opioid use disorder	Opioid withdrawal may occur when EFV is initiated in patients who are on a stable dose of methadone. Clinical monitoring is recommended, because medications used to treat opioid dependence may need to be adjusted in some patients.	EFV reduces methadone concentrations and may lead to withdrawal symptoms. See the drug–drug interaction tables (Tables 24a, 24b, and 24d) for dosing recommendations.
	Cardiac QTc interval prolongation	Consider avoiding EFV- or RPV-based regimens if the patient is taking other medications with known risk of Torsades de Pointes or in patients at higher risk of Torsades de Pointes.	High EFV or RPV concentrations may cause QT prolongation.
	High cardiac risk	Consider avoiding ABC-based regimens. If a boosted PI is the desired option, an ATV-based regimen may have advantages over a DRV-based regimen. Refer to Hyperlipidemia, below, for regimens associated with more favorable lipid profiles.	An increased risk of CV events with ABC has been observed in some studies. Observational cohort studies reported an association between some PIs (DRV and LPV/r) and an increased risk of CV events; this risk has not been seen with ATV (see Protease Inhibitor-Based Regimens). Further study is needed. Certain ARV regimens are associated with more favorable lipid profiles than other regimens, although evidence on whether this improves CV outcomes is lacking.

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	Hyperlipidemia	The Following ARV Drugs Have Been Associated With Dyslipidemia: • PI/r or PI/c • EFV • EVG/c BIC, DOR, DTG, RAL, and RPV have fewer lipid effects. TDF lowers lipids; therefore, switching from TDF to TAF is associated with increased lipids.	TDF has been associated with lower lipid levels than ABC or TAF.
	Patients with history of poor adherence to non-ARV medications or inconsistent engagement in care	Consider using regimens with a boosted PI or BIC or DTG.	These regimens have a high genetic barrier to resistance.
	Pregnancy	Refer to the Perinatal Guidelines for further guidance on ARV use during pregnancy.	
Presence of Coinfections	HBV infection	Avoid regimens that do not contain NRTIs. 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 mutations can emerge rapidly when these drugs are used without another drug that is active against HBV.
	HCV treatment required	Refer to recommendations in Hepatitis C Virus/HIV Coinfection, with special attention to potential interactions between ARV drugs and HCV drugs.	
	Treating TB with rifamycin antibiotics (rifabutin, rifampin, and rifapentine)	Recommended regimens may require dose adjustment. See the drug–drug interaction tables (Table 24a, Table 24b, Table 24c, Table 24d, and Table 24e) and Tuberculosis/HIV Coinfection for information on ARV use with rifamycin antibiotics.	Rifamycin antibiotics are inducers of CYP3A4 and UGT1A1 enzymes, causing significant decreases in concentrations of PIs, INSTIs, and RPV.

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

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