

Table 9. Advantages and Disadvantages of Antiretroviral Components of Initial Antiretroviral Therapy Recommended for Most People With HIV or for Certain Clinical Scenarios

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Note: All drugs within an ARV class are listed in alphabetical order. Information based on [Recommended Initial Regimens for Most People With HIV](#) and [Initial Antiretroviral Regimens for Certain Clinical Scenarios](#). See [Adverse Effects of Antiretroviral Medications](#) for additional details.

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
Dual NRTI	ABC/3TC	<ul style="list-style-type: none"> Coformulated with DTG Generic formulations are available for ABC/3TC, ABC, and 3TC. 	<ul style="list-style-type: none"> 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. Evidence increasingly supports a relationship between ABC and major CV events.
	TAF/FTC	<ul style="list-style-type: none"> 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 CrCl ≥ 30 mL/min Can be used in people on chronic hemodialysis without dose adjustment 	<ul style="list-style-type: none"> See text in the NRTI and Weight Gain sections regarding weight changes with TAF when compared with TDF.
	TDF/3TC	<ul style="list-style-type: none"> Active against HBV; a recommended dual-NRTI option for people with HBV/HIV coinfection Coformulated with DOR Generic formulations are available for TDF, 3TC, or TDF/3TC. 	<ul style="list-style-type: none"> Not recommended for people with CrCl < 60 mL/min. The coformulated products are not recommended for CrCl < 50 mL/min or hemodialysis. Renal toxicity is associated with TDF use, 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 is associated with TDF use, especially when combined with pharmacologic boosters.

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	TDF/FTC	<ul style="list-style-type: none"> Active against HBV; a recommended dual-NRTI option for people with HIV/HBV coinfection TDF is associated with lower lipid levels than TAF. 	<ul style="list-style-type: none"> Not recommended in people with CrCl <60 mL/min, but if used, requires dose adjustment for CrCl <50 mL/min. The coformulated tablet is not recommended if CrCl <30 mL/min or on hemodialysis. Renal toxicity is associated with TDF use, 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 is associated with TDF use, especially when combined with pharmacologic boosters.
Single NRTI	3TC or FTC	<ul style="list-style-type: none"> 3TC is coformulated with DTG as STR Avoids potential toxicities associated with TDF, TAF, or ABC use (as coformulation) 	<ul style="list-style-type: none"> DTG/3TC, DTG + FTC, and boosted DRV + (3TC or FTC) are not recommended for individuals— <ul style="list-style-type: none"> With HBV coinfection, unless on another HBV active drug (i.e., entecavir) With unknown HBV serostatus Without genotypic resistance testing results In whom rapid ART initiation is planned
INSTI	BIC	<ul style="list-style-type: none"> Coformulated with TAF/FTC No food requirement 	<ul style="list-style-type: none"> 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 the Liverpool HIV Drug Interaction Checker. CYP3A4 and UGT1A1 substrate; monitor for drug–drug interactions. See the Liverpool HIV Drug Interaction Checker. Depression and suicidal ideation have been rarely observed (usually in people with preexisting psychiatric conditions). See text in the INSTI and Weight Gain sections regarding weight gain and INSTI use.

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	DTG	<ul style="list-style-type: none"> Coformulated with ABC/3TC and 3TC as STR No food requirement Less impacted by CYP3A4-mediated interactions than BIC Favorable lipid profile 	<ul style="list-style-type: none"> 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 the Liverpool HIV Drug Interaction Checker. CYP3A4 (minor) and UGT1A1 substrate; monitor for drug interactions. See the Liverpool HIV Drug Interaction Checker. Depression and suicidal ideation have been rarely observed (usually in people with preexisting psychiatric conditions). See text in the INSTI and Weight Gain sections regarding weight gain and INSTI use.
NNRTI	DOR	<ul style="list-style-type: none"> Coformulated with TDF/3TC Fewer CNS side effects compared to EFV and RPV No food requirement Potentially higher barrier to resistance than other NNRTIs (but not comparable to that of boosted PIs or second-generation INSTIs) 	<ul style="list-style-type: none"> Monitor for CYP drug interactions. See the Liverpool HIV Drug Interaction Checker.
	RPV	<ul style="list-style-type: none"> Coformulated with TAF/FTC 	<ul style="list-style-type: none"> Not recommended in people with pre-ART HIV RNA >100,000 copies/mL or CD4 counts <200 cells/mm³ because of higher risk for virologic failure. Depression and suicidality QTc interval prolongation; consider using an alternative to RPV in people with higher risk of Torsades de Pointes, whether due to concomitant medications, prolonged QTc, or other risk factors. Rash Transmitted drug resistance is more common than with PIs and INSTIs. More NNRTI-, TDF-, and 3TC-associated mutations at virologic failure than with regimens that contain EFV and two NRTIs

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			<ul style="list-style-type: none"> • Monitor for CYP drug interactions (see the Liverpool HIV Drug Interaction Checker). • Meal requirement • Requires acid for adequate absorption <ul style="list-style-type: none"> ◦ Contraindicated with PPIs. ◦ Use with H2 antagonists or antacids with caution.
PI	DRV/c or DRV/r	<ul style="list-style-type: none"> • Higher barrier to resistance than NNRTIs • PI resistance at the time of treatment failure is uncommon with PK-enhanced PIs. 	<ul style="list-style-type: none"> • CYP3A4 inhibitors and substrates; monitor for drug interactions. See the Liverpool HIV Drug Interaction Checker. • Skin rash • Food requirement with dosing • GI adverse effects • Increased CVD risk reported in one observational cohort study^a • Hepatotoxicity has been reported, especially in those with preexisting liver disease.
	DRV/c Specific considerations	<ul style="list-style-type: none"> • Coformulated as DRV/c and DRV/c/TAF/FTC 	<ul style="list-style-type: none"> • 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. • DRV/c-based regimens are not recommended as initial therapy in pregnancy because levels of COBI and DRV are lower in the second and third trimesters. If women who are pregnant with suppressed viral load on DRV/c-based regimens elect to continue on the drug, frequent viral load monitoring is recommended.

^a D:A:D international prospective multicohort study¹

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; CrCl = creatinine clearance; CV = cardiovascular; CVD = cardiovascular disease risk; CYP = cytochrome P450; DOR = doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; 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; RPV = rilpivirine; RTV = ritonavir; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; UGT = uridine diphosphate glucuronosyltransferase

References

1. Ryom L, Lundgren JD, El-Sadr W, et al. Cardiovascular disease and use of contemporary protease inhibitors: the D:A:D international prospective multicohort study. *Lancet HIV*. 2018;5(6):e291-e300. Available at: <https://pubmed.ncbi.nlm.nih.gov/29731407>.