## 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<br>• 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.<br>• 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<br>• Active against HBV; a recommended dual-NRTI option for people with HBV/HIV coinfection<br>• Smaller decline in renal function, less proteinuria, and smaller reductions in BMD than TDF/FTC<br>• Approved for people with eGFR ≥30 mL/min<br>• Can be used in people on chronic hemodialysis | • See text in the NRTI section regarding weight gain with TAF. |
| | TDF/3TC | • Coformulated with DOR<br>• Generic formulations are available for TDF, 3TC, or TDF/3TC.<br>• Long-term clinical experience<br>• Active against HBV | • Renal toxicity, including proximal tubulopathy and acute or chronic renal insufficiency, especially when combined with pharmacologic boosters<br>• Osteomalacia has been reported as a consequence of proximal tubulopathy.<br>• 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<br>• 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<br>• Osteomalacia has been reported as a consequence of proximal tubulopathy. |

**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) |
|---|---|---|---|
| | | | • Decreased BMD has been associated with use of TDF, especially when combined with pharmacologic boosters. |
| Single NRTI | 3TC | • Coformulated with DTG as STR<br>• 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<br>• Higher barrier to resistance than EVG and RAL<br>• 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.<br>• CYP3A4 and UGT1A1 substrate (but not a CYP3A4 inducer or inhibitor); potential for drug–drug interactions.<br>• See text in the INSTI section regarding weight gain and INSTI use. |
| | DTG | • Higher barrier to resistance than EVG or RAL<br>• Coformulated with ABC/3TC and 3TC as STR<br>• No food requirement<br>• Minimal CYP3A4 interactions<br>• 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.<br>• UGT1A1 substrate; potential for drug interactions (see Table 24d)<br>• Depression and suicidal ideation (rare; usually in people with preexisting psychiatric conditions)<br>• See text in the INSTI section regarding weight gain and INSTI use. |
| NNRTI | DOR | • Coformulated with TDF/3TC<br>• Fewer CNS side effects compared to EFV and RPV<br>• No food requirement | • Shorter-term clinical experience than with RPV<br>• Potential for CYP450 drug interactions (see Tables 24b, 25a, and 25b)<br>• Treatment-emergent DOR resistance mutations may confer resistance to certain NNRTIs. |

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|---|---|---|---|
| | 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.<br>• Depression and suicidality<br>• 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.<br>• Rash<br>• Transmitted resistance is more common than with PIs and INSTIs.<br>• More NNRTI-, TDF-, and 3TC-associated mutations at virologic failure than with regimens that contain EFV and two NRTIs<br>• Potential for CYP450 drug interactions (see Tables 24b and 25a)<br>• Meal requirement (>390 kcal)<br>• Requires acid for adequate absorption<br>o Contraindicated with PPIs.<br>o Use with H2 antagonists or antacids with caution (see Table 24a for detailed dosing information). |
| PI | DRV/c<br>or<br>DRV/r | • Higher barrier to resistance than NNRTIs<br>• PI resistance at the time of treatment failure is uncommon with PK-enhanced PIs. | • Skin rash<br>• Food requirement<br>• GI adverse effects<br>• CYP3A4 inhibitors and substrates: potential for drug interactions (see Table 24a)<br>• Increased CV risk reported in one observational cohort study[a]<br>• Hepatotoxicity has been reported, especially in those with preexisting liver disease. |
| | DRV/c<br>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.<br>• Coadministration with TDF is not recommended in people with CrCl <70 mL/min. |

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|---|---|---|---|
| | | | • COBI (like RTV) is a potent CYP3A4 inhibitor, which can result in significant interactions with CYP3A substrates.<br>• 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

## 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.