



## Second-Line ART After Treatment Failure or for Regimen Simplification

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**Table 4: Antiretroviral Medications by Level of Genetic Barrier to Resistance [a,b]**

Low Resistance (single mutation)	Intermediate Resistance (1 or 2 mutations)	High Resistance (>2 mutations)
<ul style="list-style-type: none"> <li>Lamivudine</li> <li>Emtricitabine</li> <li>Efavirenz</li> <li>Nevirapine</li> <li>Rilpivirine</li> <li>Raltegravir</li> <li>Elvitegravir</li> </ul>	<ul style="list-style-type: none"> <li>Tenofovir disoproxil fumarate</li> <li>Tenofovir alafenamide</li> <li>Zidovudine</li> <li>Abacavir</li> <li>Doravirine</li> <li>Cabotegravir</li> <li>Fostemsavir</li> <li>Enfuvirtide</li> </ul>	<ul style="list-style-type: none"> <li>Etravirine</li> <li>Dolutegravir</li> <li>Bictegravir</li> <li>Darunavir [c]</li> <li>Atazanavir [c]</li> <li>Maraviroc</li> </ul>

**Notes:**

- a. Derived from [Tang and Shafer 2012; Lataillade, et al. 2018; Oliveira, et al. 2018]
- b. For group M, subtype B HIV
- c. Combined with ritonavir or cobicistat

**Table 5: ART Options After First-Line Treatment Failure With Single-Class Drug Resistance [a]**

Failed First-Line Regimen Drug Classes	Classes and Medication Options for Switch
2 NRTIs + 1 NNRTI [a]	<ul style="list-style-type: none"> <li>2 NRTIs + 1 boosted PI:               <ul style="list-style-type: none"> <li>TAF/FTC/DRV/COBI (single tablet)</li> <li>TAF/FTC + DRV/RTV</li> </ul> </li> <li>2 NRTIs + 1 INSTI:               <ul style="list-style-type: none"> <li>TAF/FTC/BIC (single tablet)</li> <li>TAF/FTC + DTG</li> </ul> </li> </ul>
2 NRTIs + 1 PI [a]	<ul style="list-style-type: none"> <li>2 NRTIs + 1 INSTI:               <ul style="list-style-type: none"> <li>TAF/FTC/BIC (single tablet)</li> <li>TAF/FTC + DTG</li> </ul> </li> <li>1 INSTI + 1 NNRTI: RPV/DTG (single tablet)</li> <li>2 NRTIs + 1 twice-daily boosted PI</li> </ul>
2 NRTIs + 1 INSTI [a]	<ul style="list-style-type: none"> <li>2 NRTIs + 1 boosted PI:               <ul style="list-style-type: none"> <li>TAF/FTC/DRV/COBI (single tablet)</li> <li>TAF/FTC + DRV/RTV</li> </ul> </li> </ul>
Multiclass	<ul style="list-style-type: none"> <li>2 NRTIs + 1 INSTI + 1 boosted PI +/- 1 NNRTI (based on genotype):               <ul style="list-style-type: none"> <li>Consider: MVC [b], FTR, IBA, LEN, ETR, DOR, RPV, TPV</li> </ul> </li> </ul>

**Abbreviations:** ART, antiretroviral therapy; BIC, bictegravir; COBI, cobicistat; DOR, doravirine; DRV, darunavir; DTG, dolutegravir; ETR, etravirine; FTC, emtricitabine; FTR, fostemsavir; IBA, ibalizumab; INSTI, integrase strand transfer inhibitor; LEN, lenacapavir; MVC, maraviroc; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; PI, protease inhibitor; RAM, resistance-associated mutation; RPV, rilpivirine; RTV, ritonavir; TAF, tenofovir alafenamide; TPV, tipranavir.

**Notes:**

- a. Single-class resistance, with no major NRTI RAMs other than M184V
- b. If current tropism assay indicates exclusive R5 tropic virus

**Box: Antiretroviral Medication Classes in Order of Position in Interruption of HIV Life Cycle**

- **Attachment inhibitors:** Fostemsavir (FTR; Rukobia), ibalizumab (IBA; Trogarzo)
- **Coreceptor antagonist:** Maraviroc (MVC; Selzentry)
- **Fusion inhibitor:** Enfuvirtide (T20; Fuzeon)
- **Capsid inhibitor:** Lenacapavir (LEN, Sunlenca)
- **Nucleoside/nucleotide reverse transcriptase inhibitors:** Abacavir (ABC; Ziagen), emtricitabine (FTC; Emtriva), lamivudine (3TC; Epivir), tenofovir (TFV)
- **Non-nucleoside reverse transcriptase inhibitors:** Doravirine (DOR; Pifeltro), efavirenz (EFV; Sustiva), etravirine (ETR; Intelence), rilpivirine (RPV; Edurant)
- **Integrase strand transfer inhibitors:** Bictegravir (BIC; Biktarvy), dolutegravir (DTG; Tivicay), raltegravir (RAL; Isentress), elvitegravir/cobicistat (EVG/COBI; Genvoya or Stribild), cabotegravir (CAB; Cabenuva)
- **Protease inhibitors:** Atazanavir (ATV; Reyataz), darunavir (DRV; Prezista), ritonavir (RTV; Norvir; as a pharmacokinetic booster), tipranavir (TPV; Aptivus)

**References**

- Lataillade M, Zhou N, Joshi SR, et al. Viral drug resistance through 48 weeks, in a phase 2b, randomized, controlled trial of the HIV-1 attachment inhibitor prodrug, fostemsavir. *J Acquir Immune Defic Syndr* 2018;77(3):299-307. [PMID: 29206721] <https://pubmed.ncbi.nlm.nih.gov/29206721>
- Oliveira M, Ibanescu RI, Anstett K, et al. Selective resistance profiles emerging in patient-derived clinical isolates with cabotegravir, bictegravir, dolutegravir, and elvitegravir. *Retrovirology* 2018;15(1):56. [PMID: 30119633] <https://pubmed.ncbi.nlm.nih.gov/30119633>
- Tang MW, Shafer RW. HIV-1 antiretroviral resistance: scientific principles and clinical applications. *Drugs* 2012;72(9):e1-25. [PMID: 22686620] <https://pubmed.ncbi.nlm.nih.gov/22686620>