

**Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy (Updated January 29, 2008)**

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ARV Class	ARV Agent(s)	Advantages	Disadvantages
NNRTIs (in alphabetical order)		<p><b>NNRTI Class Advantages:</b></p> <ul style="list-style-type: none"> <li>• Save PI options for future use</li> <li>• Long half-lives</li> <li>• Less metabolic toxicity (hyperlipidemia, insulin resistance) than with some PIs</li> </ul>	<p><b>NNRTI Class Disadvantages:</b></p> <ul style="list-style-type: none"> <li>• Low genetic barrier to resistance (single mutation confers resistance): greater risk for resistance with failure or treatment interruption</li> <li>• Cross resistance among approved NNRTIs</li> <li>• Skin rash</li> <li>• Potential for CYP450 drug interactions (See <a href="#">Tables 20–22b</a>)</li> <li>• Transmitted resistance to NNRTIs more common than resistance to PIs</li> </ul>
	<b>Efavirenz (EFV)</b>	<ul style="list-style-type: none"> <li>• Antiretroviral activity equivalent or superior to all comparators to date</li> <li>• Low pill burden; once-daily dosing</li> <li>• Fixed-dose combination with tenofovir + emtricitabine</li> </ul>	<ul style="list-style-type: none"> <li>• Neuropsychiatric side effects</li> <li>• Teratogenic in nonhuman primates, contraindicated in first trimester of pregnancy; avoid use in women with pregnancy potential</li> <li>• Lower CD4 cell count response than with LPV/r</li> </ul>
	<b>Nevirapine (NVP)</b>	<ul style="list-style-type: none"> <li>• No food effect</li> <li>• Less lipid effects than EFV</li> </ul>	<ul style="list-style-type: none"> <li>• Higher incidence of rash than with other NNRTIs, including rare but serious hypersensitivity reactions (Stevens-Johnson syndrome or toxic epidermal necrolysis)</li> <li>• Higher incidence of hepatotoxicity than with other NNRTIs, including serious and even fatal cases of hepatic necrosis</li> <li>• Treatment-naïve, female patients and treatment-naïve patients with high pre-NVP CD4 counts (&gt;250 cells/mm<sup>3</sup> females, &gt;400 cells/mm<sup>3</sup> males) are at higher risk for symptomatic hepatic events. NVP not recommended in these patients unless benefit clearly outweighs risk</li> <li>• Less clinical trial data than with EFV</li> </ul>
PIs (in alphabetical order)		<p><b>PI Class Advantage:</b></p> <ul style="list-style-type: none"> <li>• Save NNRTI for future use</li> <li>• Higher genetic barrier to resistance</li> <li>• PI resistance uncommon with failure (boosted PIs)</li> </ul>	<p><b>PI Class Disadvantages:</b></p> <ul style="list-style-type: none"> <li>• Metabolic complications (fat accumulation, dyslipidemia, insulin resistance)</li> <li>• Gastrointestinal side effects</li> <li>• Liver toxicity (especially with chronic hepatitis B or C)</li> <li>• CYP3A4 inhibitors &amp; substrates: potential for drug interactions (more pronounced w/ RTV-based regimens) (See <a href="#">Tables 20–22b</a>)</li> <li>• PR interval prolongation: generally inconsequential unless combined with another drug with similar effect</li> <li>• Absorption depends on food and low gastric pH; contraindicated with proton pump inhibitors; separate doses with antacids or H2 blockers</li> </ul>
	<b>Atazanavir (unboosted) (ATV)</b>	<ul style="list-style-type: none"> <li>• Less adverse effect on lipids than other PIs</li> <li>• Once-daily dosing</li> <li>• Low pill burden (two pills per day)</li> <li>• Good GI tolerability</li> </ul>	<ul style="list-style-type: none"> <li>• Indirect hyperbilirubinemia sometimes leading to jaundice or scleral icterus</li> <li>• Nephrolithiasis</li> <li>• PR interval prolongation: generally inconsequential unless combined with another drug with similar effect</li> <li>• Reduced drug exposure when used with TDF and EFV: need addition of RTV (ATV 300mg QD + RTV 100mg QD)</li> <li>• Absorption depends on food and low gastric pH; should not be used with proton pump inhibitors; separate doses with antacid or H2 blockers</li> </ul>
	<b>Atazanavir/ritonavir (ATV/r)</b>	<ul style="list-style-type: none"> <li>• RTV-boosting: higher trough ATV concentration and greater antiviral effect</li> <li>• Once-daily dosing</li> <li>• Low pill burden (two pills per day)</li> <li>• Low risk for PI resistance with failure</li> </ul>	<ul style="list-style-type: none"> <li>• Similar and potentially more side effects than unboosted atazanavir</li> <li>• Potentially more adverse effect on lipids than unboosted ATV</li> <li>• More hyperbilirubinemia and jaundice than unboosted ATV</li> <li>• Most efficacy data in treatment-experienced patients</li> <li>• Absorption depends on food and low gastric pH; separate doses with antacid or H2 blockers</li> <li>• In treatment-naïve patients only – can use with proton pump inhibitor in a dose no higher than omeprazole 20mg once daily taken approximately 12 hours prior to ritonavir-boosted ATV</li> </ul>
	<b>Fosamprenavir (unboosted) (FPV)</b>	<ul style="list-style-type: none"> <li>• No food effect</li> </ul>	<ul style="list-style-type: none"> <li>• Skin rash</li> <li>• Potential for PI resistance with failure, including selection of mutations resistance to darunavir</li> <li>• Gastrointestinal intolerance (higher incidence with once-daily than with twice-daily dosing)</li> <li>• Metabolic toxicity (dyslipidemia, insulin resistance)</li> </ul>

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ARV Class	ARV Agent(s)	Advantages	Disadvantages
PIs (cont'd, in alphabetical order)	Fosamprenavir/ritonavir (FPV/r)	<ul style="list-style-type: none"> <li>Twice-daily dosing resulted in efficacy comparable to LPV/r</li> <li>RTV-boosting: higher trough FPV concentration and greater antiviral effect</li> <li>Once-daily dosing possible</li> <li>No food effect</li> <li>Low risk for PI resistance with failure</li> </ul>	<ul style="list-style-type: none"> <li>Skin rash</li> <li>Once-daily dosing results in lower FPV concentrations than twice-daily dosing</li> <li>Metabolic toxicity (dyslipidemia, insulin resistance)</li> </ul>
	Lopinavir/ritonavir (LPV/r)	<ul style="list-style-type: none"> <li>Coformulated as Kaletra®</li> <li>Potential for once-daily dosing in treatment-naïve patients</li> <li>No food restriction with oral tablet formulation</li> <li>Recommended PI in pregnant women</li> <li>Greater CD4 T-cell count increase than with EFV-based regimens</li> <li>Low risk for PI resistance with failure</li> </ul>	<ul style="list-style-type: none"> <li>Gastrointestinal intolerance (higher incidence with once-daily than twice-daily dosing)</li> <li>Metabolic toxicity (dyslipidemia, insulin resistance)</li> <li>Preliminary data: lower drug exposure in pregnant women</li> <li>Once-daily dosing: lower trough concentration than BID and greater failure rates in patients with viral load &gt;100,000 copies/mL</li> </ul>
	Saquinavir + ritonavir (SQV/r)	<ul style="list-style-type: none"> <li>Data from GEMINI study show efficacy similar to LPV/r</li> <li>Alternative PI in pregnant women</li> </ul>	<ul style="list-style-type: none"> <li>Gastrointestinal intolerance</li> <li>Higher pill burden than for other PI regimens (6/day)</li> </ul>
Dual NRTIs		<ul style="list-style-type: none"> <li>Established backbone of combination antiretroviral therapy</li> </ul>	<ul style="list-style-type: none"> <li>Rare but serious cases of lactic acidosis with hepatic steatosis reported (d4T&gt;ddI=ZDV&gt;TDF=ABC=3TC=FTC)</li> </ul>
Dual-NRTI pairs (in alphabetical order)	Abacavir + lamivudine (ABC + 3TC)	<ul style="list-style-type: none"> <li>Non-inferior to ZDV+ 3TC with regard to virologic responses</li> <li>Better CD4 T-cell count response than with ZDV/3TC</li> <li>Once-daily dosing</li> <li>Coformulation (Epzicom®)</li> <li>No food effect</li> <li>No cumulative TAM-mediated resistance</li> </ul>	<ul style="list-style-type: none"> <li>Potential for abacavir systemic hypersensitivity reaction in patients with HLA-B*5701</li> </ul>
	Didanosine + lamivudine (ddI + 3TC) or Didanosine + emtricitabine (ddI + FTC)	<ul style="list-style-type: none"> <li>Once-daily dosing</li> <li>No cumulative TAM-mediated resistance</li> </ul>	<ul style="list-style-type: none"> <li>Didanosine: peripheral neuropathy, pancreatitis</li> <li>Food effect: needs to be taken on an empty stomach</li> <li>Requires dosing separation from most PIs</li> <li>Increase in toxicities when used with ribavirin, tenofovir, stavudine, or hydroxyurea</li> <li>Lack of comparative data with other standard dual-NRTI combinations</li> </ul>
	Tenofovir/emtricitabine (or lamivudine) (TDF/FTC or 3TC)	<ul style="list-style-type: none"> <li>Good virologic response when used with efavirenz; superior to AZT/3TC + EFV</li> <li>Once-daily dosing</li> <li>No food effect</li> <li>Coformulated as Truvada™ (TDF/FTC) and Atripla™ (EFV/TDF/FTC)</li> <li>No cumulative TAM-mediated resistance</li> <li>TDF/FTC: less M184V than AZT/3TC, less K65R than TDF + 3TC</li> </ul>	<ul style="list-style-type: none"> <li>Tenofovir: potential for renal impairment</li> <li>Interactions with: <ol style="list-style-type: none"> <li>ATV: TDF reduces ATV levels; need to add low dose RTV</li> <li>ddI: TDF increases ddI level; need to reduce ddI dose (combination not recommended)</li> </ol> </li> </ul>
	Zidovudine + lamivudine (ZDV + 3TC)	<ul style="list-style-type: none"> <li>Extensive experience</li> <li>Coformulated as Combivir®</li> <li>No food effect (though better tolerated with food)</li> <li>Gradual accumulation of resistance: early failure associated with M184V only</li> </ul>	<ul style="list-style-type: none"> <li>Bone marrow suppression, especially anemia, with ZDV</li> <li>Gastrointestinal intolerance</li> <li>Mitochondrial toxicity, including lipoatrophy, lactic acidosis, hepatic steatosis</li> <li>Inferior to TDF/FTC in combination with EFV</li> <li>Less CD4 T-cell response compared with ABC/3TC</li> <li>Greater selection of M184V than with TDF/FTC</li> </ul>
	Emtricitabine (in place of lamivudine)	<ul style="list-style-type: none"> <li>Longer half-life than lamivudine</li> <li>Once-daily dosing</li> <li>Coformulation with TDF (Truvada™) and with EFV/TDF (Atripla™)</li> <li>TDF/FTC: less M184V than AZT/3TC, less K65R than TDF + 3TC</li> </ul>	<ul style="list-style-type: none"> <li>Hyperpigmentation/skin discoloration</li> </ul>