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Table 12b. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy

ARV Class	Antiretroviral Agent(s)	Advantages	Disadvantages
NNRTIs		**NNRTI Class Advantages:** • Less fat maldistribution and dyslipidemia than PI-based regimens • Save PI options for future use	**NNRTI Class Disadvantages:** • Low genetic barrier to resistance • Cross-resistance among NNRTIs • Skin rash • Potential for CYP450 drug interactions
	Efavirenz	• Potent antiretroviral activity • Low pill burden and frequency (1 tablet per day)	• Neuropsychiatric side effects • Teratogenic in nonhuman primates, contraindicated in pregnancy and avoid use in women with pregnant potential
	Nevirapine	• More safety experience in pregnant women with no evidence of increase adverse hepatic events in women who received single dose nevirapine for prevention of mother to child transmission (PMTCT) • No food effect	• Higher incidence of rash than with other NNRTIs, including rare serious hypersensitivity reaction • Higher incidence of hepatotoxicity than with other NNRTIs; including serious cases of hepatic necrosis • Female patients and patients with high CD4+ T cell count (> 250 cells/mm^3 in female & > 400 cells/mm^3 in male) are at higher risk of symptomatic hepatic events
PIs		**PI Class Advantage:** • NNRTI options saved for future use • Longest prospective study data including data on survival benefit	**PI Class Disadvantages:** • Metabolic complications - fat maldistribution, dyslipidemia, insulin resistance • CYP3A4 inhibitors & substrates – potential for drug interactions (esp. with ritonavir-based regimens)
	Lopinavir/ ritonavir	• Potent antiretroviral activity • Co-formulated as Kaletra®	• Gastrointestinal intolerance • Hyperlipidemia • Little experience in pregnant women • Food requirement
	Atazanavir	• Less adverse effect on lipids than other PIs • Once daily dosing • Low pill burden	• Hyperbilirubinemia (indirect) • PR interval prolongation – generally inconsequential unless combined with another drug with similar effect (see **Table 17**) • Interaction with tenofovir and efavirenz –avoid concomitant use unless combined with RTV (ATV 300mg qd + RTV 100mg qd) • Food requirement
	Fosamprenavir	• Lower pill burden than amprenavir • No food effect	• Skin rash (19% in clinical trials)
	Fosamprenavir/ ritonavir	• Lower pill burden than amprenavir/ritonavir • Once daily regimen available • No food effect	• Skin rash (19% in clinical trials)
	Indinavir (not recommended as initial PI)	• Long-term virologic and immunologic efficacy experience	• 3-times-daily dosing and food restriction reduced adherence • High fluid intake required (1.5–2 liters of fluid per day) • Nephrolithiasis
	Indinavir/ ritonavir	• Low-dose ritonavir ↑ indinavir $T_{1/2}$ & Cmin allows for twice-daily instead of 3-times-daily dosing • Eliminates food restriction of indinavir	• Possibly higher incidence of nephrolithiasis than with IDV alone • High fluid intake required (1.5–2 liters of fluid per day)
	Nelfinavir	• More extensive experience in pregnant women than with other PIs	• Diarrhea • Higher rate of virologic failure than with other PIs in comparative trials • Food requirement
	Saquinavir (hgc or sgc) + ritonavir	• Low-dose ritonavir reduces saquinavir daily dose and frequency -↑ Cmax, Cmin, & $T_{1/2}$	• Gastrointestinal intolerance (sgc worse than hgc)

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Table 12b. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy

ARV Class	Antiretroviral Agent(s)	Advantages	Disadvantages
NRTIs		• Established backbone of combination antiretroviral therapy	• Rare but serious cases of lactic acidosis with hepatic steatosis reported with most NRTIs
Triple NRTI regimen	Abacavir + zidovudine (or stavudine) + lamivudine only	• Abacavir + zidovudine + lamivudine - Co-formulated as Trizivir® • Minimal drug-drug interactions • Low pill burden • Saves PI & NNRTI for future option	• Inferior virologic response when compared to efavirenz-based and indinavir-based regimens • Potential for abacavir hypersensitivity reaction
Dual NRTIs: backbone of three or more drug combination therapy	Zidovudine + lamivudine	• Most extensive and favorable virological experience • Co-formulated as Combivir®– ease of dosing • No food effect • Lamivudine – minimal side effects	• Bone marrow suppression with zidovudine • Gastrointestinal intolerance
	Stavudine + lamivudine	• No food effect • Once-daily dosing (when extended release stavudine formulation becomes available)	**Adverse effects associated with stavudine:** • Peripheral neuropathy, lipoatrophy, hyperlactatemia and lactic acidosis, reports of progressive ascending motor weakness, potential for hyperlipidemia • Higher incidence of mitochondrial toxicity with stavudine than with other NRTIs
	Tenofovir + lamivudine	• Good virologic response when used with efavirenz • Well tolerated • Once-daily dosing	• Tenofovir – reports of renal impairment
	Didanosine + lamivudine	• Once-daily dosing	• Peripheral neuropathy, pancreatitis – associated with didanosine • Food effect – needs to be taken on an empty stomach
	Abacavir + lamivudine	• No food effect • Study showing non-inferior to zidovudine + lamivudine as 2-NRTI backbone	• Potential for abacavir systemic hypersensitivity reaction
	NRTI + emtricitabine (in place of lamivudine)	• Long half-life of emtricitabine allows for once daily dosing (of emtricitabine)	