

TREATMENT TOXICITY

While adverse effects from HAART are common, they can usually be managed symptomatically while continuing the HAART regimen without interruption, as most adverse effects associated with antiretroviral agents resolve within one to three months of initiation of therapy. If the adverse effect is severe enough to require modification of the regimen, substitution of the offending drug with another antiretroviral agent is an option if it can be reasonably deduced which agent is responsible for the side effect in question. *Table 8* presents options for drug substitution in the event of selected common adverse reactions. Consultation with an expert HIV clinician is strongly recommended when a regimen change is necessary.

Table 8: Common Adverse Drug Reactions Associated with First-Line HAART Regimens and Recommended Drug Substitutions¹

REGIMEN	TOXICITY	DRUG SUBSTITUTION
d4T/3TC/NVP	• d4T-related neuropathy or pancreatitis	• Switch d4T → AZT
	• d4T-related lipodystrophy	• Switch d4T → TDF or ABC ²
	• NVP-related severe hepatotoxicity	• Switch NVP → EFV ³
	• NVP-related severe rash (but not life-threatening)	• Switch NVP → EFV [‡]
	• NVP-related life-threatening rash (e.g. Stevens-Johnson syndrome)	• Switch NVP → PI ⁴
AZT/3TC/NVP	• AZT-related persistent GI intolerance or severe haematological toxicity	• Switch AZT → d4T
	• NVP-related severe hepatotoxicity	• Switch NVP → EFV [‡]
	• NVP-related severe rash (but not life-threatening)	• Switch NVP → EFV [‡]
	• NVP-related life-threatening rash (e.g. Stevens-Johnson syndrome)	• Switch NVP → PI [§]
d4T/3TC/EFV	• d4T-related neuropathy or pancreatitis	• Switch d4T → AZT
	• d4T-related lipodystrophy	• Switch d4T → TDF or ABC [†]
	• EFV-related persistent CNS toxicity	• Switch EFV → NVP
AZT/3TC/EFV	• AZT-related persistent GI intolerance or severe haematological toxicity	• Switch AZT → d4T
	• EFV-related persistent CNS toxicity	• Switch EFV → NVP

¹Adapted from the World Health Organisation. Table C: Major potential toxicities of first-line ARV regimens recommended drug substitutions in Revised WHO guidelines for scaling up antiretroviral therapy in resource-limited settings. 2003 revision. Available at: http://www.who.int/hiv/pub/prev_care/en/arvrevision2003en.pdf.

²Switching out d4T appears to reduce, and may even reverse, lipodystrophy (though very slowly). TDF and ABC represent the best alternatives to d4T in this setting, but their availability in the Caribbean is limited; AZT is a reasonable alternative where TDF and ABC are not available.

³**Except in pregnancy.** If the patient is pregnant or at risk for becoming pregnant, substitute a PI (preferred) or ABC.

⁴Recommended PIs include LPV/r or SQV/r; NFV and IDV/r are acceptable alternatives.

Occasionally, severe HAART-related toxicity requires discontinuation of all ARV agents. In such circumstances, it is best to discontinue all of the medications simultaneously, because continuation of therapy with only one or two ARV agents is associated with the development of drug resistance. If the HAART regimen being discontinued contains an NNRTI (e.g. NVP or EFV), some expert clinicians would recommend discontinuing the NNRTI three to seven days prior to discontinuing the NRTIs, owing to the prolonged plasma half-life of NNRTIs. HAART should be withheld until the patient recovers, at which time re-initiation of therapy with a different regimen can be considered in consultation with an HIV expert.