

Table 18. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations

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18b. Adverse Events With Potential Long-Term Complications (in alphabetical order)

Adverse effects	Causative ARVs	Onset/clinical manifestation	Estimated frequency	Risk Factors	Prevention/monitoring	Management
Cardiovascular effects	Possibly PIs and other ARVs with unfavorable effects on lipids (e.g. EFV, d4T)	<u>Onset:</u> months to years after beginning of therapy <u>Presentation:</u> premature coronary artery disease	3–6 per 1,000 patient-years	Other risk factors for cardiovascular disease such as smoking, age, hyperlipidemia, hypertension, diabetes mellitus, family history of premature coronary artery disease, and personal history of coronary artery disease	<ul style="list-style-type: none"> Assess each patient's cardiac risk factors Consider non-PI based regimen Monitor & identify patients with hyperlipidemia or hyperglycemia Counseling for life style modification: smoking cessation, diet, and exercise 	<ul style="list-style-type: none"> Early diagnosis, prevention, and pharmacologic management of other cardiovascular risk factors such as hyperlipidemia, hypertension, and insulin resistance/diabetes mellitus Assess cardiac risk factors Lifestyle modifications: diet, exercise, and/or smoking cessation Switch to agents with less propensity for increasing cardiovascular risk factors, i.e., NNRTI- or ATV-based regimen & avoid d4T use
Hyperlipidemia	All PIs (except ATV); d4T; EFV (to a lesser extent)	<u>Onset:</u> weeks to months after beginning of therapy <u>Presentation:</u> <u>All PIs except ATV:</u> ↑ in LDL & total cholesterol (TC) & triglyceride (TG), ↓ in HDL <u>LPV/r & RTV:</u> disproportionate ↑ in TG <u>d4T:</u> mostly ↑ in TG; may also have ↑ in LDL & total cholesterol (TC) <u>EFV or NVP:</u> ↑ in HDL, slight ↑ TG	Varies with different agents <u>Swiss Cohort:</u> ↑TC & TG – 1.7–2.3x higher in patients receiving (non-ATV) PI	<ul style="list-style-type: none"> Underlying hyperlipidemia Risk based on ARV therapy PI: LPV/r & RTV - boosted PIs > NFV & APV > IDV > ATV; NNRTI: EFV more common than NVP NRTI: d4T most common 	<ul style="list-style-type: none"> Use non-PI, non-d4T based regimen Use ATV-based regimen Fasting lipid profile at baseline, 3–6 months after starting new regimen, then annually or more frequently if indicated (in high-risk patients, or patients with abnormal baseline levels) 	<ul style="list-style-type: none"> Follow HIVMA/ACTG guidelines for management [394] Assess cardiac risk factor Lifestyle modification: diet, exercise, and/or smoking cessation Switching to agents with less propensity for causing hyperlipidemia <p><u>Pharmacologic Management:</u></p> <ul style="list-style-type: none"> ↑ total cholesterol, LDL, TG 200–500mg/dL: “statins” – pravastatin or atorvastatin (See Tables 20 & 21 for drug interaction information) TG >500mg/dL: gemfibrozil or micronized fenofibrate
Insulin resistance/ Diabetes mellitus	All PIs	<u>Onset:</u> weeks to months after beginning of therapy <u>Presentation:</u> Polyuria, polydipsia, polyphagia, fatigue, weakness; exacerbation of hyperglycemia in patients with underlying diabetes	Up to 3%–5% of patients developed diabetes in some series	<ul style="list-style-type: none"> Underlying hyperglycemia, family history of diabetes mellitus 	<ul style="list-style-type: none"> Use PI-sparing regimens Fasting blood glucose 1–3 months after starting new regimen, then at least every 3–6 months 	<ul style="list-style-type: none"> Diet and exercise Consider switching to an NNRTI-based regimen Metformin “Glitazones” Sulfonylurea Insulin
Osteonecrosis	All PIs	<u>Clinical Presentation (generally similar to non-HIV population):</u> <ul style="list-style-type: none"> Insidious in onset, with subtle symptoms of mild to moderate periarticular pain 85% of the cases involving one or both femoral heads, but other bones may also be affected Pain may be triggered by weight bearing or movement 	Reported incidence on the rise <u>Symptomatic osteonecrosis:</u> 0.08%–1.33%; <u>Asymptomatic osteonecrosis:</u> 4% from MRI reports	<ul style="list-style-type: none"> Diabetes Prior steroid use Old age Alcohol use Hyperlipidemia Role of ARVs and osteonecrosis – still controversial 	<ul style="list-style-type: none"> Risk reduction (e.g., limit steroid and alcohol use) Asymptomatic cases w/ <15% bony head involvement – follow with MRI every 3–6 months x 1 yr, then every 6 months x 1 yr, then annually – to assess for disease progression 	<p><u>Conservative management:</u></p> <ul style="list-style-type: none"> ↓ weight bearing on affected joint; Remove or reduce risk factors Analgesics as needed <p><u>Surgical Intervention:</u></p> <ul style="list-style-type: none"> Core decompression +/- bone grafting – for early stages of disease For more severe and debilitating disease – total joint arthroplasty