



Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV

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Adverse Effects of Antiretroviral Agents (Last updated October 25, 2018; last reviewed October 25, 2018)

Adverse effects have been reported with all ARV drugs and, in the earlier era of combination ART, adverse effects were among the most common reasons for switching or discontinuing therapy and for medication nonadherence.¹ Fortunately, newer ARV regimens are associated with fewer serious and intolerable adverse effects than regimens used in the past. Generally, less than 10% of ART-naïve patients enrolled in randomized trials experience treatment-limiting adverse events. However, the long-term complications of ART can be underestimated, because most clinical trials use highly specific inclusion criteria when enrolling participants and the duration of participant follow-up is relatively short. As ART is now recommended for all patients regardless of CD4 cell count, and because therapy must be continued indefinitely, the focus of patient management has evolved from identifying and managing early ARV-related toxicities to individualizing therapy to avoid long-term adverse effects, including diabetes, accelerated vascular disease, kidney dysfunction, and bone loss. To achieve sustained viral suppression over a lifetime, both long-term and short-term ART toxicities must be anticipated and overcome. The clinician must consider potential adverse effects when selecting an ARV regimen, as well as the individual patient's comorbidities, concomitant medications, and prior history of drug intolerances.

Several factors may predispose individuals to adverse effects of ARV medications, such as:

- Concomitant use of medications with overlapping and additive toxicities.
- Comorbid conditions that increase the risk of or exacerbate adverse effects. For example, underlying liver disease from alcohol use, co-infection with viral hepatitis, and/or liver steatosis^{2,3} may increase the risk of hepatotoxicity when drugs such as efavirenz (EFV) or protease inhibitors are used; psychiatric disorders may be exacerbated by EFV, rilpivirine, and, infrequently, by integrase strand transfer inhibitors;^{4,5} and borderline or mild renal dysfunction increases the risk of nephrotoxicity from tenofovir disoproxil fumarate (TDF).
- Drug-drug interactions that may increase toxicities of ARV drugs or concomitant medications.
- Genetic factors that predispose patients to abacavir (ABC) hypersensitivity reaction,^{6,7} EFV neuropsychiatric toxicity and QTc prolongation,^{8,9} and atazanavir (ATV)-associated hyperbilirubinemia.¹⁰

Information on the adverse effects of ARVs is outlined in several tables in the guidelines. Table 15 provides clinicians with a list of the most common and/or severe ARV-associated adverse events for each drug class. The most common adverse effects of individual ARV agents are summarized in [Appendix B, Tables 1–6](#).

Table 15. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy (page 1 of 5)

“N/A” indicates either that there are no reported cases for that particular side effect or that data for that specific ARV drug class are not available. See [Appendix B](#) for additional information listed by drug.

Adverse Effect	Drug Class				
	NRTIs	NNRTIs	PIs	INSTIs	EIs
Bleeding Events	N/A	N/A	Spontaneous bleeding, hematuria in hemophilia <u>TPV</u> : Intracranial hemorrhage is associated with CNS lesions, trauma, alcohol abuse, hypertension, coagulopathy, anticoagulant or antiplatelet agents, and the use of vitamin E supplements.	N/A	N/A
Bone Density Effects	<u>TDF</u> : Associated with greater loss of BMD than other NRTIs. Osteomalacia may be associated with renal tubulopathy and urine phosphate wasting. <u>TAF</u> : Associated with smaller declines in BMD than those seen with TDF.	Decreases in BMD observed after the initiation of any ART regimen.			N/A
Bone Marrow Suppression	<u>ZDV</u> : Anemia, neutropenia	N/A	N/A	N/A	N/A
Cardiac Conduction Effects	N/A	<u>RPV, EFV</u> : QTc prolongation	<u>SQV/r, ATV/r, and LPV/r</u> : PR prolongation. Risk factors include pre-existing heart disease and the use of other medications. <u>SQV/r</u> : QT prolongation. Obtain ECG before administering SQV.	N/A	N/A
Cardiovascular Disease	<u>ABC and ddI</u> : Associated with an increased risk of MI in some cohort studies. Absolute risk greatest in patients with traditional CVD risk factors.	N/A	<u>DRV, FPV, IDV, and LPV/r</u> : Associated with cardiovascular events in some cohorts	N/A	N/A
Cholelithiasis	N/A	N/A	<u>ATV</u> : Cholelithiasis and kidney stones may present concurrently. Median onset is 42 months.	N/A	N/A

Table 15. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy (page 2 of 5)

Adverse Effect	Drug Class				
	NRTIs	NNRTIs	PIs	INSTIs	EIs
Diabetes Mellitus and Insulin Resistance	ZDV, d4T, and ddI	N/A	Reported for some (IDV, LPV/r), but not all, PIs.	N/A	N/A
Dyslipidemia	d4T > ZDV > ABC: ↑ TG and LDL TAF: ↑ TG, ↑ LDL, ↑ HDL (no change in TC:HDL ratio) TDF has been associated with lower lipid levels than ABC or TAF.	EFV: ↑ TG, ↑ LDL, ↑ HDL	All RTV- or COBI-Boosted PIs: ↑ TG, ↑ LDL, ↑ HDL LPV/r and FPV/r > DRV/r and ATV/r: ↑ TG	EVG/c: ↑ TG, ↑ LDL, ↑ HDL	N/A
Gastrointestinal Effects	ddI and ZDV > Other NRTIs: Nausea and vomiting ddI: Pancreatitis	N/A	GI intolerance (e.g., diarrhea, nausea, vomiting) NFV and LPV/r > DRV/r and ATV/r: Diarrhea	EVG/c: Nausea and diarrhea	IBA: 8% of patients reported diarrhea in a study of 40 people.
Hepatic Effects	Reported with most NRTIs. <u>ZDV, d4T, and ddI</u> : Steatosis ddI: Prolonged exposure linked to noncirrhotic portal hypertension and esophageal varices. <u>When TAF, TDF, 3TC, and FTC are Withdrawn in Patients with HBV/HIV Coinfection or When HBV Resistance Develops</u> : Patients with HBV/HIV coinfection may develop severe hepatic flares.	EFV: Most cases relate to an increase in transaminases. Fulminant hepatitis leading to death or hepatic failure requiring transplantation have been reported. NVP: Severe hepatotoxicity associated with skin rash or hypersensitivity. A 2-week NVP dose escalation may reduce risk. Risk is greater for women with pre-NVP CD4 counts >250 cells/mm ³ and men with pre-NVP CD4 counts >400 cells/mm ³ . NVP should never be used for post-exposure prophylaxis. EFV and NVP are not recommended in patients with hepatic insufficiency (Child-Pugh class B or C).	All PIs: Drug-induced hepatitis and hepatic decompensation have been reported; greatest frequency occurs with TPV/r. TPV/r: Contraindicated in patients with hepatic insufficiency (Child Pugh class B or C). IDV and ATV: Jaundice due to indirect hyperbilirubinemia	N/A	MVC: Hepatotoxicity with or without rash or HSRs reported.

Table 15. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy (page 3 of 5)

Adverse Effect	Drug Class				
	NRTIs	NNRTIs	PIs	INSTIs	EIs
<p>Hypersensitivity Reaction</p> <p>Excluding rash alone or Stevens-Johnson syndrome</p>	<p>ABC: Contraindicated if patient is HLA-B*5701 positive.</p> <p>Median onset for HSR is 9 days; 90% of reactions occur within first 6 weeks of treatment.</p> <p><u>HSR Symptoms (in Order of Descending Frequency):</u> Fever, rash, malaise, nausea, headache, myalgia, chills, diarrhea, vomiting, abdominal pain, dyspnea, arthralgia, and respiratory symptoms</p> <p>Symptoms worsen with continuation of ABC.</p> <p>Patients should not be rechallenged with ABC if HSR is suspected, regardless of their HLA-B*5701 status.</p>	<p>NVP: Hypersensitivity syndrome of hepatotoxicity and rash that may be accompanied by fever, general malaise, fatigue, myalgias, arthralgias, blisters, oral lesions, conjunctivitis, facial edema, eosinophilia, renal dysfunction, granulocytopenia, or lymphadenopathy.</p> <p>Risk is greater for ARV-naive women with pre-NVP CD4 counts >250 cells/mm³ and men with pre-NVP CD4 counts >400 cells/mm³. Overall, risk is higher for women than men.</p> <p>A 2-week dose escalation of NVP reduces risk.</p>	N/A	<p>RAL: HSR reported when RAL is given with other drugs also known to cause HSRs. All ARVs should be stopped if HSR occurs.</p> <p>DTG: Reported in <1% of patients in clinical development program</p>	<p>MVC: HSR reported as part of a syndrome related to hepatotoxicity.</p>
<p>Lactic Acidosis</p>	<p><u>Reported with NRTIs, Especially d4T, ZDV, and ddI:</u> Insidious onset with GI prodrome, weight loss, and fatigue. May rapidly progress with tachycardia, tachypnea, jaundice, weakness, mental status changes, pancreatitis, and organ failure. Mortality high if serum lactate >10 mmol/L.</p> <p>Women and obese patients at increased risk.</p>	N/A	N/A	N/A	N/A
<p>Lipodystrophy</p>	<p><u>Lipoatrophy:</u> d4T > ZDV. More likely when NRTIs are coadministered with EFV than with an RTV-boosted PI.</p>	<p><u>Lipohypertrophy:</u> Trunk fat increase observed with EFV-, PI-, and RAL-containing regimens; however, causal relationship has not been established.</p>			N/A

Table 15. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy (page 4 of 5)

Adverse Effect	Drug Class				
	NRTIs	NNRTIs	PIs	INSTIs	EIs
Myopathy/ Elevated Creatine Phosphokinase	<u>ZDV</u> : Myopathy	N/A	N/A	<u>RAL</u> and <u>DTG</u> : ↑ CPK, rhabdomyolysis, and myopathy or myositis have been reported.	N/A
Nervous System/ Psychiatric Effects	<u>d4T</u> > <u>ddI</u> : Peripheral neuropathy (can be irreversible) <u>d4T</u> : Associated with rapidly progressive, ascending neuromuscular weakness resembling Guillain-Barré syndrome (rare)	Neuropsychiatric Events: EFV > RPV, DOR > ETR <u>EFV</u> : Somnolence, insomnia, abnormal dreams, dizziness, impaired concentration, depression, psychosis, and suicidal ideation. Symptoms usually subside or diminish after 2–4 weeks. Bedtime dosing may reduce symptoms. Risk factors include presence of psychiatric illness, concomitant use of agents with neuropsychiatric effects, and increased EFV concentrations because of genetic factors or increased absorption with food. An association between EFV and suicidal ideation, suicide, and attempted suicide was found in a retrospective analysis of comparative trials. <u>RPV</u> : Depression, suicidality, sleep disturbances <u>DOR</u> : Sleep disorders and disturbances, dizziness, altered sensorium; depression and suicidality/self-harm	N/A	All INSTIs : Insomnia, depression, and suicidality have been reported with INSTI use, primarily in patients with pre-existing psychiatric conditions.	N/A
Rash	<u>FTC</u> : Hyperpigmentation	All NNRTIs	ATV, DRV, FPV, LPV/r, and TPV	All INSTIs	MVC, IBA

Table 15. Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy (page 5 of 5)

Adverse Effect	Drug Class				
	NRTIs	NNRTIs	PIs	INSTIs	EIs
Renal Effects/ Urolithiasis	<p><u>TDF</u>: ↑ SCr, proteinuria, hypophosphatemia, urinary phosphate wasting, glycosuria, hypokalemia, and non-anion gap metabolic acidosis. Concurrent use of TDF with COBI- or RTV-containing regimens appears to increase risk.</p> <p><u>TAF</u>: Less impact on renal biomarkers and lower rates of proteinuria than TDF.</p>	<p><u>RPV</u>: Inhibits Cr secretion without reducing renal glomerular function.</p>	<p><u>ATV and LPV/r</u>: Associated with increased risk of chronic kidney disease in a large cohort study.</p> <p><u>IDV</u>: ↑ SCr, pyuria, renal atrophy, or hydronephrosis</p> <p><u>IDV, ATV</u>: Stone or crystal formation. Adequate hydration may reduce risk.</p> <p><u>COBI (as a Boosting Agent for DRV or ATV)</u>: Inhibits Cr secretion without reducing renal glomerular function.</p>	<p><u>DTG, COBI (as a Boosting Agent for EVG), and BIC</u>: Inhibits Cr secretion without reducing renal glomerular function</p>	<p><u>IBA</u>: SCr abnormalities ≥Grade 3 reported in 10% of trial participants.</p>
Stevens-Johnson Syndrome/ Toxic Epidermal Necrosis	<p>Some reported cases for ddl and ZDV.</p>	<p>NVP > DLV, EFV, ETR, RPV</p>	<p>Some reported cases for FPV, DRV, IDV, LPV/r, and ATV.</p>	<p>RAL</p>	<p>N/A</p>

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; ART= antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/r = atazanavir/ritonavir; **BIC = bicitgravir**; BMD = bone mineral density; CD4 = CD4 T lymphocyte; Cr = creatinine; CNS = central nervous system; COBI = cobicistat; CPK = creatine phosphokinase; CVD = cardiovascular disease; d4T = stavudine; ddl = didanosine; DLV = delavirdine; **DOR = doravirine**; DRV = darunavir; DRV/r = darunavir/ritonavir; DTG = dolutegravir; ECG = electrocardiogram; EFV = efavirenz; EI = entry inhibitor; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FPV = fosamprenavir; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; GI = gastrointestinal; HBV = hepatitis B virus; HDL = high-density lipoprotein; HSR = hypersensitivity reaction; **IBA = ibalizumab**; IDV = indinavir; INSTI = integrase strand transfer inhibitor; LDL = low-density lipoprotein; LPV/r = lopinavir/ritonavir; MI = myocardial infarction; MVC = maraviroc; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SCr = serum creatinine; SQV = saquinavir; SQV/r = saquinavir/ritonavir; TAF = tenofovir alafenamide; TC = total cholesterol; TDF = tenofovir disoproxil fumarate; TG = triglycerides; TPV = tipranavir; TPV/r = tipranavir/ritonavir; ZDV = zidovudine

Switching Antiretroviral Therapy Due to Adverse Effects

Some patients experience treatment-limiting toxicities associated with ART. In these cases, ART must be modified. ART-associated adverse events can range from acute and potentially life-threatening to chronic and insidious. Serious life-threatening events (e.g., hypersensitivity reaction due to ABC, symptomatic hepatotoxicity, or severe cutaneous reactions) require the immediate discontinuation of all ARV drugs and re-initiation of an alternative regimen without overlapping toxicity. Toxicities that are not life-threatening (e.g., urolithiasis with ATV or renal tubulopathy with TDF) can usually be managed by substituting another ARV agent for the presumed causative agent without interrupting ART. Other chronic, non-life-threatening adverse events (e.g., dyslipidemia) can be addressed either by switching the potentially causative agent for another agent or by managing the adverse event with additional pharmacological or nonpharmacological interventions. Management strategies must be individualized for each patient.

Switching from an effective ARV regimen (or agent) to a new regimen (or agent) must be done carefully and only when the potential benefits of the change outweigh the potential complications of altering treatment. The fundamental principle of regimen switching is to maintain viral suppression. When selecting a new agent or regimen, providers should be aware that resistance mutations are archived in HIV reservoirs, regardless of when the mutations were identified by genotypic resistance testing. Even if resistance mutations are absent from subsequent resistance test results, they may reappear under selective drug pressure. It is critical that providers review the following information before implementing any treatment switch:

- The patient's medical and complete ARV history, including prior virologic responses to ART;
- All previous resistance test results;
- Viral tropism (if MVC is being considered);
- HLA-B*5701 status (if ABC is being considered);
- Comorbidities;
- The patient's pregnancy status, ability to use effective contraceptives, and desire for pregnancy (if DTG is being considered for patients of child-bearing potential);
- HBV status, since patients with evidence of chronic HBV infection should not discontinue TDF or TAF unless a regimen contains another agent that is active against HBV;
- Adherence history;
- Prior intolerances to any ARVs; and
- Concomitant medications and supplements, taking into consideration any potential drug interactions with ARVs.

A patient's willingness to accept new requirements for food or dosing must also be assessed. In some cases, medication costs may also be a factor to consider before switching treatment. Signs and symptoms of comorbidities, adverse effects of concomitant medications, or HIV itself may mimic adverse effects caused by ART. Therefore, clinicians should investigate all potential causes for an adverse event. In the case of a severe adverse event, it may be necessary to discontinue or switch ARVs pending the outcome of such an investigation. For the first few months after an ART switch, the patient should be closely monitored for any new adverse events. The patient's viral load should also be monitored to assure continued viral suppression.

Table 16 lists several major ART-associated adverse events and the options for appropriate switches between agents in an ARV regimen. The table focuses on the ARVs most commonly used in the United States and lists substitutions that are supported by ARV switch studies, the findings of comparative ARV trials and observational cohort studies, or expert opinion. Switching agents in a successful ARV regimen should be done carefully and only when the potential benefits of the change outweigh the potential complications of altering treatment.

Table 16. Antiretroviral Therapy-Associated Adverse Events That Can Be Managed with Substitution of Alternative Antiretroviral Agent (page 1 of 3)

Adverse Event	ARV Agent(s) or Drug Class		Comments
	Switch from	Switch to	
Bone Density Effects	TDF ^a	TAF or ABC ^b NRTI-sparing regimens or regimens using only 3TC or FTC as the NRTI may be considered, if appropriate.	Declines in BMD have been observed upon initiation of most ART regimens. Switching from TDF to alternative ARV agents has been shown to increase bone density, but the clinical significance of this increase remains uncertain. TAF is associated with smaller declines in BMD than TDF, and patients show improvement in BMD upon switching to TAF. The long-term impact of TAF on patients with osteopenia or osteoporosis is unknown; close clinical monitoring is recommended in this setting.
Bone Marrow Suppression	ZDV	TDF, TAF, or ABC ^b	ZDV has been associated with neutropenia and macrocytic anemia.
Cardiac QTc Interval Prolongation	EFV, RPV	A PI- or INSTI-based regimen	High EFV and RPV exposures may cause QT prolongation. Consider switching from EFV- or RPV-based regimens if patient is taking other medications with known risk of Torsades de Pointes, or in patients at higher risk of Torsades de Pointes.
Cardiovascular Events Myocardial infarction, ischemic stroke	ABC	TDF, TAF, FTC, or 3TC	ABC use has been associated with CV disease and cardiac events in some, but not all, observational studies. TDF has been associated with lower lipid levels than TAF.
	RTV- or COBI-boosted PI regimens, EFV, EVG/c	RAL, DTG, BIC , or RPV	RAL, DTG, BIC , and RPV have less effect on lipids than RTV- or COBI-boosted PI regimens, EFV, and EVG/c. Large observation cohorts have found an association between some PIs (DRV, FPV, IDV, LPV/r) and an increased risk of CV events. However, this association has not been seen with ATV. Further study is needed.
Central Nervous System, Neuropsychiatric Side Effects Dizziness, suicidal ideation, abnormal dreams, depression	EFV, RPV	ETR, PI/c, or PI/r INSTIs may be used, but monitoring is recommended (see Comments column).	In most patients, EFV-related CNS effects subside within 4 weeks after initiation of the drug. Persistent or intolerable effects should prompt substitution of EFV. INSTIs are associated with insomnia. Depression and suicidality have been infrequently reported with INSTI use, primarily in patients with pre-existing psychiatric conditions.
Dyslipidemia Hypertriglyceridemia (with or without elevated LDL level)	RTV- or COBI-boosted regimens, and EFV	RAL, DTG, BIC , or RPV	Elevated TG and LDL levels are more common with LPV/r and FPV/r than with other RTV-boosted PIs. Improvements in TG and LDL levels have been observed with switch from LPV/r to ATV or ATV/r. ^c

Table 16. Antiretroviral Therapy-Associated Adverse Events That Can Be Managed with Substitution of Alternative Antiretroviral Agent (page 2 of 3)

Adverse Event	ARV Agent(s) or Drug Class		Comments
	Switch from	Switch to	
Gastrointestinal Effects Nausea, diarrhea	LPV/r	ATV/c, ATV/r, DRV/c, DRV/r, RAL, DTG, BIC , or EVG/c	GI intolerance is common with boosted PIs and is linked to the total dose of RTV. More GI toxicity is seen with LPV/r than with ATV/r or DRV/r. GI effects are often transient and do not warrant substitution unless they are persistent and intolerable.
	Other RTV- or COBI-boosted regimens	RAL, DTG, BIC , or NNRTIs	In a trial of treatment-naïve patients, rates of diarrhea and nausea were similar for EVG/c/TDF/FTC and ATV/r plus TDF/FTC.
Hypersensitivity Reaction	ABC	TDF or TAF	Never rechallenge with ABC following a suspected HSR, regardless of the patient's HLA-B*5701 status.
	NVP, EFV, ETR, RPV	Non-NNRTI ART	Risk of HSR with NVP is higher for women and those with high CD4 cell counts.
	DTG, RAL	Non-INSTI ART	Reactions to NVP, ETR, RAL, DTG, and MVC may be accompanied by elevated liver transaminases.
	MVC	Suitable alternative ART	
Insulin Resistance	LPV/r, FPV/r	INSTI, NNRTI	Results of switch studies have been inconsistent. Studies in HIV-negative patients suggest a direct causal effect of LPV/r (and IDV) on insulin resistance. However, traditional risk factors may be stronger risk factors for insulin resistance than the use of any PI.
Jaundice and Icterus	ATV, ATV/c, ATV/r	DRV/c, DRV/r, INSTI, or NNRTI	Increases in unconjugated bilirubin are common with ATV and generally do not require modification of therapy unless resultant symptoms are distressing to the patient.
Lipoatrophy Subcutaneous fat wasting of limbs, face, buttocks	d4T, ZDV	TDF, TAF, or ABC ^b	Peripheral lipoatrophy is associated with prior thymidine analog (d4T and ZDV) use. Switching from these ARVs prevents worsening lipoatrophy, but fat recovery is typically slow (may take years) and incomplete.
Lipohypertrophy	Accumulation of visceral, truncal, dorsocervical, and breast fat has been observed during ART, particularly during use of older PI-based regimens (e.g., IDV), but whether ART directly causes fat accumulation remains unclear. There is no clinical evidence that switching to another first line regimen will reverse weight or visceral fat gain.		
Rash	NNRTIs (especially NVP and EFV)	PI- or INSTI-based regimen	Mild rashes that develop after initiation of NNRTIs other than NVP rarely require treatment switch. When serious rash develops due to any NNRTI, switch to another drug class.
	DRV/c, DRV/r	ATV/c, ATV/r, or another drug class (e.g., INSTI)	Mild rashes following DRV/r use may resolve without modification of therapy. For more severe reactions, change to an alternative boosted PI or an agent from another drug class.

Table 16. Antiretroviral Therapy-Associated Adverse Events That Can Be Managed with Substitution of Alternative Antiretroviral Agent (page 3 of 3)

Adverse Event	ARV Agent(s) or Drug Class		Comments
	Switch from	Switch to	
Renal Effects Including proximal renal tubulopathy and elevated creatinine	TDF ^a	ABC, ^b TAF (for patients with CrCl >30 mL/min), NRTI-sparing regimens, or regimens using only 3TC or FTC as the NRTI may be considered if appropriate.	TDF may cause tubulopathy. Switching from TDF to TAF is associated with improvement in proteinuria and renal biomarkers. The long-term impact of TAF on patients with pre-existing renal disease, including overt proximal tubulopathy, is unknown, and close clinical monitoring is recommended in this setting.
	ATV/c, ATV/r, LPV/r	DTG, BIC , RAL, or NNRTI	COBI, DTG, BIC , and, to a lesser extent, RPV, can increase SCr through inhibition of creatinine secretion. This effect does not affect glomerular filtration. However, assess patient for renal dysfunction if SCr increases by >0.4 mg/dL.
Stones Nephrolithiasis and cholelithiasis	ATV, ATV/c, ATV/r	DRV/c, DRV/r, INSTI, or NNRTI	This switch should be made if the clinician believes ATV is the cause of the stones.

^a In patients with chronic active HBV infection, another agent that is active against HBV should be substituted for TDF.

^b ABC should be used only in patients known to be HLA-B*5701 negative.

^c TDF reduces ATV levels; therefore, unboosted ATV should not be coadministered with TDF.

Key to Acronyms: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; **BIC** = bictegravir; BMD = bone mineral density; CD4 = CD4 T lymphocyte; CNS = central nervous system; COBI = cobicistat; CrCl = creatine clearance; CV = cardiovascular; d4T = stavudine; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FPV = fosamprenavir; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; GI = gastrointestinal; HBV = hepatitis B virus; HSR = hypersensitivity reaction; IDV = indinavir; INSTI = integrase strand transfer inhibitor; LDL = low-density lipoprotein; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SCr = serum creatinine; TAF = tenofovir alafenamide; TC = total cholesterol; TDF = tenofovir disoproxil fumarate; TG = triglycerides; ZDV = zidovudine

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