

Table 17i. Antiretroviral Therapy–Associated Adverse Effects and Management Recommendations—Nephrotoxic Effects

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Adverse Effects	Associated ARVs	Onset/Clinical Manifestations	Estimated Frequency	Risk Factors	Prevention/Monitoring	Management
Urolithiasis/ Nephrolithiasis	ATV DRV causes crystalluria, but it is not associated with nephrolithiasis.	Onset - Weeks to months after starting therapy Presentation - Crystalluria - Hematuria - Pyuria - Flank pain - Increased creatinine levels in some cases	ATV-related nephrolithiasis occurs in <10% of patients and has been reported after stopping ATV.	In adults, elevated urine pH (>5.7) The risk factors in children are unknown.	Prevention - Maintain adequate hydration. Monitoring - Obtain urinalysis at least every 6–12 months.	Provide adequate hydration and pain control. Consider using another ARV drug in place of ATV.
Renal Dysfunction	TDF	Onset - Variable; in adults, renal dysfunction may occur weeks to months after initiating therapy. - Hypophosphatemia appears at a median of 18 months. - Glucosuria may occur after 1 year of therapy. - Abnormal urine protein/osmolality ratio may be an early indicator.	Adults - Approximately 2% of adults experience increased serum creatinine levels. - Approximately 0.5% of adults experience severe renal complications.	Risk May Increase in Children With the Following Characteristics - Aged >6 years - Black race, Hispanic/Latino ethnicity - Advanced HIV infection	Monitor urine protein, urine glucose, and serum creatinine at 3- to 6-month intervals. Some Panel members routinely monitor serum phosphate levels in patients who are taking TDF.	If TDF is the likely cause, consider using an alternative ARV drug. TAF has significantly less renal toxicity than TDF. Changing from TDF to TAF may improve renal function and has been shown to be safe.

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		Presentation <i>More Common</i> - Increased serum creatinine levels, proteinuria, and normoglycemic glucosuria - Increased urinary protein/creatinine ratio and albumin/creatinine ratio - Hypophosphatemia, usually asymptomatic; may present with bone and muscle pain or muscle weakness <i>Less Common</i> - Renal failure, acute tubular necrosis, Fanconi syndrome, proximal renal tubulopathy, interstitial nephritis, and nephrogenic diabetes insipidus with polyuria	Children Approximately 4% of children experience hypophosphatemia or proximal tubulopathy; frequency increases with prolonged TDF therapy and advanced HIV infection.	- Hypertension - Diabetes - Concurrent use of PIs (especially LPV/r) and preexisting renal dysfunction - Longer duration of TDF treatment - The presence of the apolipoprotein L1 variants G1 and G2 appears to increase the risk of renal abnormality in children with HIV. These alleles are more common in people of Black descent.	Measure serum phosphate if the patient experiences persistent proteinuria or glucosuria or has symptoms of bone pain, muscle pain, or weakness. Because toxicity risk increases with the duration of TDF treatment, do not decrease the frequency of monitoring over time.	

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Elevation in Serum Creatinine	DTG, COBI, RPV, BIC	Onset - Within 1 month of starting treatment Presentation - Asymptomatic. These drugs decrease renal tubular secretion of creatinine, leading to an increase in serum creatinine levels without a true change in eGFR. - Clinicians need to distinguish between a true change in eGFR and other causes. A true change may be associated with other medical conditions, the continuing rise of serum creatinine levels over time, and albuminuria.	Common laboratory finding	In adults, baseline serum creatinine, male sex, TDF use, and possibly defined polymorphisms (UGT1A1). The risk factors in children are unknown.	Monitor serum creatinine. Assess for renal dysfunction if serum creatinine increases by >0.4 mg/dL or if increases continue over time.	No need to change therapy Reassure the patient about the benign nature of the laboratory abnormality.

Key: ARV = antiretroviral; ATV = atazanavir; BIC = bictegravir; COBI = cobicistat; DRV = darunavir; DTG = dolutegravir; eGFR = estimated glomerular filtration rate; LPV/r = lopinavir/ritonavir; Panel = the Panel on Antiretroviral Therapy and Medical Management of Children Living With HIV; PI = protease inhibitor; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; UGT1A1 = uridine diphosphate glucuronosyltransferase 1A1

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