## Table 15i. 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 |
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| **Urolithiasis/ Nephrolithiasis** | ATV<br><br>DRV causes crystalluria, but it is not associated with nephrolithiasis. | **Onset**<br>• Weeks to months after starting therapy<br><br>**Clinical Findings**<br>• Crystalluria<br>• Hematuria<br>• Pyuria<br>• Flank pain<br>• 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)<br><br>The risk factors in children are unknown. | **Prevention**<br>• Maintain adequate hydration.<br><br>**Monitoring**<br>• 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**<br>• Variable; in adults, renal dysfunction may occur weeks to months after initiating therapy.<br>• Hypophosphatemia appears at a median of 18 months.<br>• Glucosuria may occur after 1 year of therapy.<br>• Abnormal urine protein/osmolality ratio may | **Adults**<br>• Approximately 2% of adults experience increased serum creatinine levels.<br>• Approximately 0.5% of adults experience severe renal complications.<br><br>**Children**<br>• Approximately 4% of children experience | **Risk May Increase in Children with the Following Characteristics**<br>• Aged >6 years<br>• Black race, Hispanic/Latino ethnicity<br>• Advanced HIV infection<br>• Hypertension | 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.<br><br>Measure serum phosphate if the patient experiences persistent proteinuria | If TDF is the likely cause, consider using an alternative ARV drug. TAF has significantly less toxicity than TDF. Changing from TDF to TAF may improve renal function. |

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| | | be an early indicator.<br><br>**Presentation**<br><br>*More Common*<br><br>• Increased serum creatinine levels, proteinuria, normoglycemic glucosuria<br><br>• Increased urinary protein/creatinine ratio and albumin/creatinine ratio<br><br>• Hypophosphatemia, usually asymptomatic; may present with bone and muscle pain or muscle weakness<br><br>*Less Common*<br><br>• Renal failure, acute tubular necrosis, Fanconi syndrome, proximal renal tubulopathy, interstitial nephritis, nephrogenic diabetes insipidus with polyuria | hypophosphatemia or proximal tubulopathy; frequency increases with prolonged TDF therapy and advanced HIV infection. | • Diabetes<br><br>• Concurrent use of PIs (especially LPV/r) and preexisting renal dysfunction<br><br>• Longer duration of TDF treatment<br><br>• 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 persons of Black descent. | or glucosuria or has symptoms of bone pain, muscle pain, or weakness.<br><br>Because toxicity risk increases with the duration of TDF treatment, do not decrease the frequency of monitoring over time. | |
| **Elevation in Serum Creatinine** | DTG, COBI, RPV, BIC | **Onset**<br><br>• Within 1 month of starting treatment<br><br>**Presentation**<br><br>• Asymptomatic. These drugs decrease renal tubular secretion of creatinine, leading to an increase in serum creatinine levels without a true change in eGFR. | Common laboratory finding. | 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.<br><br>Reassure the patient about the benign nature of the laboratory abnormality. |

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| | | • 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. | | | | |

**Key:** ARV = antiretroviral; ATV = atazanavir; BIC = bictegravir; COBI = cobicistat; DRV = darunavir; DTG = dolutegravir; eGFR = estimated glomerular filtration rate; LPV/r = lopinavir/ritonavir; mg/dL = milligrams per deciliter; 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

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