Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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<td><strong>Urolithiasis/ Nephrolithiasis</strong></td>
<td>ATV, DRV causes crystalluria, but it is not associated with nephrolithiasis.</td>
<td>ATV-related nephrolithiasis occurs in &lt;10% of patients and has been reported after stopping ATV.</td>
<td>In adults, elevated urine pH (&gt;5.7). The risk factors in children are unknown.</td>
<td>Prevention: • Maintain adequate hydration. Monitoring: • Obtain urinalysis at least every 6–12 months.</td>
<td>Provide adequate hydration and pain control. Consider using another ARV drug in place of ATV.</td>
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<td><strong>Renal Dysfunction</strong></td>
<td>TDF</td>
<td>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.</td>
<td>Adults: • Approximately 2% of adults experience increased serum creatinine levels. • Approximately 0.5% of adults experience severe renal complications. Children: • Approximately 4% of children experience hypophosphatemia or proximal tubulopathy; frequency increases with prolonged TDF therapy and advanced HIV infection.</td>
<td>Risk May Increase in Children with the Following Characteristics: • Aged &gt;6 years • Black race, Hispanic/Latino ethnicity • 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 persons of black descent.</td>
<td>Monitor urine protein, urine glucose and serum creatinine at 3-month to 6-month intervals. Some Panel members routinely monitor serum phosphate levels in patients who are taking TDF. 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. If TDF is the likely cause, consider using an alternative ARV drug. TAF has significantly less toxicity than TDF.</td>
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### Table 15i. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Nephrotoxic Effects

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| Elevation in Serum Creatinine   | DTG, COBI, RPV, BIC | Onset: Within a 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. | Common              | 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 = bicitravir; COBI = cobicistat; dL = deciliter; DRV = darunavir; DTG = dolutegravir; eGFR = estimated glomerular filtration rate; LPV/r = lopinavir/ritonavir; PI = protease inhibitor; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

**References**


