### Table 15. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Nephrotoxic Effects

*Last updated April 16, 2019; last reviewed April 16, 2019*

<table>
<thead>
<tr>
<th>Adverse Effects</th>
<th>Associated ARVs</th>
<th>Onset/Clinical Manifestations</th>
<th>Estimated Frequency</th>
<th>Risk Factors</th>
<th>Prevention/Monitoring</th>
<th>Management</th>
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</table>
| **Urolithiasis/Nephrolithiasis**| ATV hadic LAS cause crystalluria, but it is not associated with nephrolithiasis.        | Onset:  
• Weeks to months after starting therapy  
Clinical Findings:  
• Crystalluria  
• Hematuria  
• Pyuria  
• Flank pain  
• Increased creatinine in some cases  
ATV-related nephrolithiasis occurs in <10% of patients.  
In adults, elevated urine pH (>5.7)  
The risk factors in children are unknown. | Provide adequate hydration and pain control. Consider using another ARV in place of ATV.  
**Prevention:**  
• Maintain adequate hydration.  
**Monitoring:**  
• Obtain urinalysis at least every 6 months–12 months. |
| **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 a year of therapy.  
• Abnormal urine protein/osmolality ratio may be an early indicator.  
Presentation  
*More Common:*  
• Increased serum creatinine, proteinuria, normoglycemic glucosuria  
• Increased urinary protein/creatinine ratio and albumin/creatinine ratio  
• Hypophosphatemia, usually asymptomatic; may present with bone and muscle pain, or muscle weakness  
*Less Common:*  
• Renal failure, acute tubular necrosis, Fanconi syndrome, proximal renal tubulopathy, interstitial nephritis, nephrogenic diabetes insipidus with polyuria  
Adults:  
• Approximately 2% experience increased serum creatinine levels.  
• Approximately 0.5% experience severe renal complications  
Children:  
• Approximately 4% experience hypophosphatemia or proximal tubulopathy; frequency increases with prolonged TDF therapy and advanced HIV infection.  
**Risk May Increase in Children with the Following Characteristics:**  
• Aged >6 years  
• Black race, Hispanic/Latino ethnicity  
• Advanced HIV infection  
• Hypertension  
• Diabetes  
• Concurrent use of PIs (especially LPV/r) and preexisting renal dysfunction  
• Risk increases with longer duration of TDF treatment.  
**Monitor urine protein, urine glucose and serum creatinine at 3-month to 6-month intervals. For patients taking TDF, some Panel members routinely monitor serum phosphate levels.  
Consider using an alternative ARV drug. TAF has significantly less toxicity than TDF.  
**If TDF is the likely cause, consider using an alternative ARV drug. TAF has significantly less toxicity than TDF.** |

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**Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection**

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Table 15i. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Nephrotoxic Effects
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<tbody>
<tr>
<td>Elevation in Serum Creatinine</td>
<td>DTG, COBI, RPV</td>
<td>Onset: • Within a month of starting treatment</td>
<td>Common 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.</td>
<td>N/A</td>
<td>Monitor serum creatinine. Assess for renal dysfunction if serum creatinine increases by &gt;0.4 mg/dL or if increases continue over time.</td>
<td>No need to change therapy. Reassure the patient about the benign nature of the laboratory abnormality.</td>
</tr>
</tbody>
</table>

Key to Acronyms: ARV = antiretroviral; ATV = atazanavir; 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


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