### Table 15i. Antiretroviral-Therapy-Associated Adverse Effects and Management Recommendations—Nephrotoxic Effects  
(Last updated May 22, 2018; last reviewed May 22, 2018)  
(page 1 of 2)

<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>
</tr>
</thead>
</table>
| **Urolithiasis/Nephrolithiasis** | ATV, IDV, DRV causes crystalluria, but it is not associated with nephrolithiasis. | **Onset:**  
  • Weeks to months after starting therapy  
  **Clinical Findings:**  
  • Crystalluria  
  • Hematuria  
  • Pyuria  
  • Flank pain  
  • Sometimes increased creatinine | ATV-related nephrolithiasis occurs in <10% of patients.  
  IDV-related nephrolithiasis occurs more often in children (29%) than adults (12.4%). | In adults, elevated urine pH (>5.7)  
  Unknown in children | **Prevention:**  
  • Maintain adequate hydration.  
  • IDV is not FDA-approved for use in children and should be avoided.  
  **Monitoring:**  
  • Obtain urinalysis at least every 6–12 months. | **Provide adequate hydration and pain control; consider using alternative ARV. If patient is on IDV, discontinue.** |
| **Renal Dysfunction** | TDF | **Onset:**  
  • Variable; in adults, weeks to months after initiation of 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. Hypophosphatemia, usually asymptomatic; may present with bone and muscle pain, weakness  
  **Less Common:**  
  • Renal failure, acute tubular necrosis, Fanconi syndrome, proximal renal tubulopathy, interstitial nephritis, nephrogenic diabetes insipidus with polyuria | Adults:  
  • Approximately 2% with increased serum creatinine  
  • Approximately 0.5% with severe renal complications  
  **Children:**  
  • Approximately 4% with hypophosphatemia or proximal tubulopathy; frequency increases with prolonged TDF therapy, advanced HIV infection, or concomitant use of ddl.  
  **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 ddl or PIs (especially LPV/r), and preexisting renal dysfunction  
  • Risk increases with longer duration of TDF treatment. | **Prevention:**  
  Monitor urine protein, glucose or urinalysis, and serum creatinine at 3- to 6-month intervals.  
  For patients taking TDF, some panelists add serum phosphate to the list of routine labs to monitor.  
  **Monitor urine protein, glucose or urinalysis, and serum creatinine at 3- to 6-month intervals.**  
  **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 duration of TDF treatment, do not decrease the frequency of monitoring over time.** | **If TDF is the likely cause, consider using alternative ARV. TAF has significantly less toxicity than TDF.**  
  **ddI is no longer recommended and should be discontinued.** |
<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>
</tr>
</thead>
<tbody>
<tr>
<td>Elevation in Serum Creatinine</td>
<td>DTG, COBI, RPV</td>
<td>Onset: Within a month of starting treatment</td>
<td>Common</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 patient about the benign nature of the laboratory abnormality.</td>
</tr>
</tbody>
</table>

**Key to Acronyms:** ARV = antiretroviral; ATV = atazanavir; COBI = cobicistat; ddI = didanosine; DRV = darunavir; DTG = dolutegravir; eGFR = estimated glomerular filtration rate; FDA = Food and Drug Administration; IDV = indinavir; LPV/r = lopinavir/ritonavir; PI = protease inhibitor; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

**References**


