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

_Last updated May 22, 2018; last reviewed May 22, 2018_ (page 1 of 2)

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<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>
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</table>
| **Urolithiasis/ Nephrolithiasis** | ATV, IDV, DRV | 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. | 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.  
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.  
**ddl is no longer recommended and should be discontinued.**
**Table 15i. Antiretroviral-Therapy-Associated Adverse Effects and Management Recommendations—Nephrotoxic Effects**

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<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**


