Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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<th>Estimated Frequency</th>
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| 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 ddI. | 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 ddI 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. | 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 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>
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### References


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**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


