Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection
Table 15k. Antiretroviral-Therapy-Associated Adverse Effects and Management Recommendations—Peripheral Nervous System Toxicity  *(Last updated May 22, 2018; last reviewed May 22, 2018)*

<table>
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<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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</thead>
<tbody>
<tr>
<td>ARV Toxic Neuropathy&lt;sup&gt;a&lt;/sup&gt;</td>
<td>d4T, ddI</td>
<td>Onset: • Weeks to months</td>
<td>Children: • Around 1% overall • 10% to 25% in children taking d4T Adults: • Up to 50% in adults taking d4T</td>
<td>• Pre-existing neuropathy • Elevated triglyceride levels • Poor nutrition • More advanced HIV disease • Concomitant use of other neurotoxic agents (e.g., INH) • Some mitochondrial DNA haplogroups may have increased risk.</td>
<td>Do not use d4T, ddI, or IDV. Co-administration of ddI and d4T is contraindicated (no exceptions).</td>
<td>Investigate potential causes, including non-ARV medications and nutritional deficiencies.</td>
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<td></td>
<td>d4T or ddI are no longer recommended for use in an ARV regimen. PIs rarely, primarily IDV</td>
<td>Presentation: • Decreased sensation • Aching, burning, painful numbness • Hyperalgesia • Allodynia • Decreased or absent ankle reflexes</td>
<td></td>
<td></td>
<td>Monitor for symptoms and signs of peripheral neuropathy. Do not use d4T, ddI, or IDV. Co-administration of ddI and d4T is contraindicated (no exceptions).</td>
<td>Discontinue offending agent. Topical capsaicin 8% may be helpful. Consider referral to a neurologist. Data are insufficient to allow the Panel to recommend use of any of the following modalities: tricyclic antidepressants, gabapentin, gregabalin, mexiletine, lamotrigine, and acupuncture or other complementary approaches.</td>
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</tbody>
</table>

<sup>a</sup> Peripheral neuropathy may be underreported in children because symptoms are difficult to evaluate in young children.

<sup>b</sup> HIV infection itself may cause a distal sensory neuropathy that is phenotypically identical to ARV toxic neuropathy.

**Key to Acronyms:** ARV = antiretroviral; d4T = stavudine; ddI = didanosine; IDV = indinavir; INH = isoniazid; PI = protease inhibitor; the Panel = The Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV

**References**


