### 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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<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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<tr>
<td>ARV Toxic Neuropathy&lt;br&gt;&lt;sup&gt;a&lt;/sup&gt;</td>
<td>d4T, ddl or d4T or ddl are no longer recommended for use in an ARV regimen. PIs rarely, primarily IDV</td>
<td>Onset:  • Weeks to months Presentation:  • Decreased sensation  • Aching, burning, painful numbness  • Hyperalgesia  • Alldynia  • Decreased or absent ankle reflexes Distribution:  • Bilateral soles of feet, ascending to legs and fingertips</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, ddl, or IDV. Co-administration of ddl and d4T is contraindicated (no exceptions). Monitor for symptoms and signs of peripheral neuropathy.</td>
<td>Investigate potential causes, including non-ARV medications and nutritional deficiencies. 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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<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.

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

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**References**


