

# **IMPORTANT: ADDENDUM TO 2006 WHO GUIDELINES ON ANTIRETROVIRAL THERAPY FOR HIV INFECTION IN ADULTS AND ADOLESCENTS**

## **NEW DOSAGE RECOMMENDATIONS FOR STAVUDINE (d4T)**

**Stavudine (d4T) is now recommended at the dose of 30 mg twice daily for all adult and adolescent patients regardless of body weight.[A-III]**

After the publication of WHO's 2006 guidelines for HIV therapy in adults and adolescents, the WHO Guidelines Development Group (GDG) reviewed evidence for the use of stavudine (d4T) at reduced doses. Previously, the preferred d4T dosing was weight-based. Dosing for patients >60 kg was recommended at 40 mg twice daily; dosing for patients <60 kg was recommended at 30 mg twice daily.

A systematic review of nine randomized trials and six observational cohort studies strongly suggests that stavudine-containing regimens maintain clinical and virologic efficacy when stavudine is dosed at 30 mg twice daily, and that this reduced dose is associated with lower rates of toxicity, especially peripheral neuropathy, compared to the 40 mg twice daily dose. Complementary studies have also demonstrated a significant reduction of mitochondrial DNA depletion in patients on the 30 mg twice daily dose. However, there are limited data available about reducing the incidence of lactic acidosis with this strategy.

**Based on available evidence, the GDG has concluded that the 30 mg formulation of stavudine, dosed twice daily, should be used for all adult and adolescent patients, irrespective of body weight.** This recommendation, which was previously considered an option, is now established as the preferred approach when d4T is used as part of an ARV therapeutic regimen.

### **Programmatic implications:**

- 1) All new patients with weight over 60 kg being prescribed a stavudine-containing regimen should be started on d4T 30 mg only. No patients already receiving d4T 30mg should be stepped up to d4T 40 mg.*
- 2) All patients receiving d4T 30 mg or 40 mg with evidence of stavudine-related toxicity (even with no signs of treatment failure) should be moved to a non-stavudine containing regimen, according to current WHO ART guidelines.*
- 3) All patients receiving d4T 40 mg without evidence of stavudine toxicity, should be moved to d4T 30 mg, as soon as possible, considering the programmatic feasibility.*
- 4) Any new procurement orders of stavudine in either single or fixed dose combinations should only include d4T 30 mg.*
- 5) Any procurement orders of d4T 40 mg in either single or fixed dose combinations should, to the extent possible, be cancelled and be replaced with d4T 30 mg containing products.*

Other technical and operational recommendations related to the clinical management of stavudine in the 2006 WHO guidelines are unchanged.

### **References:**

- Hill A, Ruxrungtham K, Hanvanich M et al. Systematic review of clinical trials evaluating low doses of stavudine as part of antiretroviral treatment. **Expert Opin Pharmacother.** 2007;8(5):679-88.
- Sánchez-Conde M, Mendoza C, Jiménez-Nacher I et al. Reductions in stavudine dose ameliorate mitochondrial-associated complications without compromising antiviral activity. **HIV Clin Trials** 2005; 6(4):1075-90.
- Wolf E, Koegl C, Hoffmann C et al. Low dose stavudine: as effective as standard dose but with less side effects. **XV International AIDS Conference, Bangkok, 11-16 July 2004** [Abstract WePe B5861].