Update: ARV dosing chart for children and adolescents, 2012

This edition of the *Southern African Journal of HIV Medicine* includes a new Antiretroviral Drug Dosing Chart for Children and Adolescents (2012). The chart was updated by the Southern African HIV Clinicians Society's ARV Dosing Committee,* a sub-group of the Society's Child and Adolescent Committee, and the National Department of Health (DoH). The purpose of the chart is to provide an accurate and reliable antiretroviral therapy (ART) dosing guide for South African practitioners initiating and managing ART in children and adolescents. The chart is intended for doctors, nurses and pharmacists working in the South African public sector.

The 2012 chart serves to update both the Antiretroviral Drug Dosing Chart for Children (2009), which was incorporated into the paediatric treatment guidelines of the DoH (Guidelines for the Management of HIV in Children[1]) in 2010, as well as the Antiretroviral Drug Dosing Chart for Children (2011) which was adopted in the Western Cape province. The 2012 chart represents national paediatric treatment policy.

In this latest revision, the following principles were considered:

- continued use of the standardised World Health Organization (WHO) weight bands[2]
- provision of target doses or dose ranges (mg/kg or mg/m^2)
- use of WHO weight-band dosing recommendations, differing where necessary, based on characteristics of currently available antiretroviral (ARV) drug formulations in the South African public sector, or local evidence-based practice, where possible
- avoidance of dosing any ARV drug below 90% of the target dose or dose range, or higher than 25% above the target dose or dose range, adjusting WHO-recommended dosing if indicated, and taking into account that younger children (beyond the neonatal period) may frequently require relatively higher doses to achieve drug exposures similar to those of older children and adults
- where evidence is available, incorporation of the option of once-daily dosing for treatment simplification, to promote adherence and support harmonisation of paediatric and adult ART regimens
- incorporation of flexibility, wherever practical and available formulations allow, by providing both liquid and solid formulation dosing recommendations for up to a 25 kg body weight, while retaining the principle of moving children from liquid to solid formulations whenever possible
- use of one formulation (either liquid or solid) for any given dose
- avoidance of different morning and evening doses for a given drug, where possible
- use of fractions of tablets (no less than half) only where available tablets are scored, and warning about which tablet formulations are film-coated and must be swallowed whole (not chewed, divided or crushed).

Significant revisions

Abacavir and lamivudine

- Dosing in the lower weight bands (<10 kg) was considered to be too high in relation to the principles described above, and has therefore been revised slightly to recommend 2 ml twice daily (bd) in the weight band 3.0 - 4.9 kg, and 3 ml bd in the weight band 5.0 - 6.9 kg.
- A liquid formulation option is provided for ≤24.9 kg of body weight. Whereas lamivudine tablets may be divided and, if necessary, crushed for easier ingestion by younger children, currently available abacavir tablets are film-coated and unscored and must be swallowed whole. This has necessitated the recommendation to use only the liquid formulation (in unavoidably large volumes) for the weight band 20.0 - 24.9 kg.
- The option of once-daily dosing is provided for 10 kg and upwards. Although there are no available clinical trial data involving children initiating ART with once-daily dosing of abacavir and lamivudine, the inclusion of this dosing option is supported by pharmacokinetic studies on clinically stable children aged 3 - 12 years with low viral loads, who were switched from twice-daily to once-daily dosing.[3-5] No treatment-limiting toxicity was reported and there was high acceptability and a strong preference for once-daily dosing among children and caregivers. This allows for the option of a once-daily treatment regimen for those children receiving efavirenz in combination with abacavir and lamivudine.

Lopinavir/ritonavir

- Dosing in the lower weight bands (<5 kg) was considered to be too high in relation to the principles described above. Taking this into account and toxicity concerns, doses have been adjusted slightly to 1 ml (80 mg) bd for 3.0 - 4.9 kg and 1.5 ml (120 mg) bd for 5.0 - 9.9 kg.
- The option of tablets in the 10.0 - 13.9 kg weight band has been removed as it is very unlikely that many children in this group would be able to swallow whole tablets, adding to the risk that caregivers may divide or crush these tablets, which must be avoided.
- The dosing for ritonavir boosting with rifampicin-based TB treatment has been adjusted accordingly and simplified to a dose of 1.5 ml (previously 1.2 ml) for the weight band 5.0 - 9.9 kg.

*The Society convened a meeting of paediatric experts on 2 December 2011, chaired by Professor Mark Cotton and Dr Tammy Meyers. The chart principles and major changes were agreed upon at this meeting. A subcommittee of meeting participants, co-ordinated by Laurie Schowalter and comprised of Dr Moherndren Archary, Dr Leon Levin, Dr James Nuttall and Liezl Pienaar, worked in partnership with the national DoH and Paediatric Essential Drug List Committee to finalise changes post meeting.

Efavirenz

- The 2012 chart recommends using 600 mg in children weighing >40 kg (the 2011 chart allowed for use of 600 mg above 35 kg).

Didanosine

- Once-daily dosing has been adopted.

Other

The 2012 chart also includes 2 additional warning statements:

(i) Avoid Kaletra® (LPV/rtv) solution in any full-term infant aged <14 days and any premature infant aged <14 days after their due date of delivery (40 weeks post conception) or obtain expert advice.

(ii) Currently available tablet formulations of abacavir, efavirenz, LPV/rtv (Aluvia®) and AZT are film-coated and must be swallowed whole and **not** chewed, divided or crushed.

The chart is available for download on the Society's website: http://www.sahivsoc.org. A limited number of hard copies are available. To request a copy while there are supplies, email: child_adolescent@sahivsoc.org.

James Nuttall
Paediatric Infectious Diseases Unit
Red Cross War Memorial Children's Hospital and University of Cape Town
james.nuttall@uct.ac.za

Laurie Schowalter
Southern African HIV Clinicians Society

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