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Therapeutic drug monitoring of lopinavir in Thai HIV infected children who received Lopinavir/ritonavir 200/50 mg tablet formulation manufactured by Matrix Laboratories Limited

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THERAPEUTIC DRUG MONITORING OF LOPINAVIR IN HUMAN IMMUNODEFICIENCY VIRUS-INFECTED CHILDREN RECEIVING ADULT TABLETS

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Abstract: Because of the lack of a lopinavir/ritonavir (LPV/r) pediatric formulation, 54 HIV-infected children were given generic LPV/r adult tablets. Of 54 children, 21 took cut pills to get the appropriate dose. The median (interquartile range) LPV trough serum concentration (Ctrough) was 6.7 (5.0 –9.9) mg/L. All the children had Ctrough 1.0 mg/L and 96% had values 4.0 mg/L. LPV/r adult tablets can be used in children when it is necessary.

Lopinavir/ritonavir (LPV/r), a potent protease inhibitor (PI) is commonly used for second-line treatment in HIV-infected children in developing countries who failed first-line non-nucleoside reverse transcription inhibitor regimen.1 Pediatric formulations are available as a liquid, a soft-gel capsule, as well as a tablet, which is heat-stable and is not affected by food. It has been reported that the tablet formulation has similar bioavailability as the soft-gel capsule, and with less pharmacokinetic variability.2 Commercial pediatric tablets of LPV/r are not yet available in Thailand, because of compulsory licensing actions taken by the Thai Ministry of Public Health.3 Currently, the generic LPV/r adult tablet formulation (200/50 mg) has replaced the original soft gel capsule for
treatment of HIV-infected adults and children in Thailand, under the Thai National AIDS Program (NAP). Because the pediatric tablet formulation is not available, pill cutting of adult tablets is necessary to obtain an appropriate dose for children, even though cutting tablets is not recommended by the manufacturer. The issue of cutting adult pills for use in children has been a challenge in resource-limited settings. For instance, the adult fixed-dose combination of stavudine/lamivudine/nevirapine has been widely used as first-line therapy for children, most often requiring pill cutting, in Thailand and many developing countries. This approach has resulted in satisfactory outcomes with acceptable pharmacokinetic profiles in Thai children.4

This study aimed to assess the serum concentration of lopinavir (LPV) by measuring trough concentrations (Ctough) in HIV-infected Thai children who were receiving generic LPV/r adult tablet compared with the Ctough while receiving the soft gel capsule. In addition, the effect of cutting LPV/r tablets in half was evaluated to ensure that the children were getting the appropriate dosage according to their weight.