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PAHO statement on removal of two AIDS medicines from list of prequalified products

On June 17 2004, two antiretroviral medicines manufactured by CIPLA Ltd. (India), Lamivudine 150mg tablets and Lamivudine 150mg / Zidovudine 300mg tablets, were removed by WHO from its list of HIV/AIDS prequalified medicines. The delisting of the product has generated some concerns in the region. PAHO/WHO recognizes that there is a need to provide clear and concise information with regard to the removal of the products from the WHO list, to avoid unnecessary alarm and interruption in treatment.

HIV/AIDS medicines approved by WHO are prequalified according to detailed and transparent procedures which are described in the reference document: 'Procedure for assessing the acceptability, in principle, of pharmaceutical products for purchase by United Nations Agencies', available at '<http://mednet3.who.int/prequal/documents/ppdoc2.pdf>'. The WHO prequalification process requires the continued assessment and reevaluation of prequalified products, and an approved product is subject to delisting if it is found that the product no longer meets quality standards initially declared. Bioequivalence is a WHO recommended requirement and quality standard for generic pharmaceutical products for which the therapeutic response can vary depending on product formulation. However, this recommended requirement has not been adopted by many countries in the region.

The data and information CIPLA had originally submitted for prequalification in the product dossiers was considered acceptable, meeting international norms and standards for quality and bioequivalence. Hence, the medicines were considered eligible for prequalification and were placed on the list. However, as part of the ongoing monitoring and verification process, an inspection was later performed at the Contract Research Organization (CRO) that was used by CIPLA to carry out the bioequivalence studies. During the inspection, compliance with Good Clinical Practices (GCP) and Good Laboratory Practices (GLP) was assessed. The data and information submitted in the product dossiers were also verified against the raw data from CRO. The CRO was found not to be compliant with GCP and GLP and the raw data failed to prove bioequivalence. As a result, WHO removed the 2 products from the list. WHO is anticipating a rapid response from CIPLA, possible by the end of July, with respect to new studies that the company has already initiated through an alternative CRO.

The two CIPLA products are still compliant with other quality standards, meeting specifications for Active Pharmaceutical Ingredients, impurity profile and formulation, and are manufactured in



compliance with Good Manufacturing Practices. In addition, the action taken by WHO does not mean that the products are not bioequivalent, but that the bioequivalence requirement for prequalification has not been determined.

In considering the above, PAHO/WHO suggests that ARV treatment that is ongoing should not be interrupted using these products until such time as the products can be substituted by other WHO prequalified antiretrovirals with the same active ingredient and strength, either using the originator product (GlaxoSmithKline) or other generic (Hetero, Ranbaxy) (http://mednet.who.int/prequal/hiv/hiv_suppliers.pdf). In doing so, continuity is ensured without interruption either in treatment or antiretroviral supply.