DHHS Panel on Antiretroviral Therapy Guidelines for Adults and Adolescents – Notice on Nelfinavir FDA-Pfizer Letter

September 13, 2007

A notice of concern was released by the FDA *[1]* and Pfizer *[2]* regarding the presence of ethyl methanesulfonate (EMS) in nelfinavir products manufactured by Pfizer and distributed in the US. Nelfinavir is an HIV protease inhibitor that is an acceptable option in regimens for treatment naïve patients, but is inferior to other preferred or alternative protease inhibitors *[3]*.

In the summer of 2007, nelfinavir manufactured by Roche Laboratories and distributed in Europe and other countries outside the US, was recalled due to the presence of high levels of EMS. EMS is a byproduct of the nelfinavir manufacturing process and is known to be an animal carcinogen, mutagen, and teratogen. As stated in the FDA and Pfizer letters, current information suggests that the level of EMS in the product from Pfizer is lower than that seen in the product manufactured by Roche. The FDA and Pfizer determined that the lower amount of EMS found in the Pfizer nelfinavir does not warrant a general recall of the drug. Even though there are no reports of harm to children and unborn fetuses, FDA and Pfizer determined that the exposure of EMS should be avoided in these patients.

Based on this new information, the DHHS Panel on Antiretroviral Therapy Guidelines for Adults and Adolescents offers the following recommendations for HIV-infected adults currently receiving nelfinavir:

- Abrupt discontinuation of nelfinavir as a result of concerns for EMS without replacing it with another effective antiretroviral agent is not recommended.

- For non-pregnant adults residing in the US who are currently receiving nelfinavir as part of an effective combination antiretroviral regimen, therapy should either be continued as is or switched to another effective regimen.

- Nelfinavir use should be avoided in HIV-infected women during pregnancy and/or anticipating conception; for detailed recommendations, please refer to the DHHS Perinatal and Pediatric Panels' Notice on Nelfinavir FDA-Pfizer Letter *[4, 5]*

1. Food and Drug Administration. Viracept (nelfinavir mesylate) and guidance on use in pregnant women and pediatric patients due to the presence of ethyl methanesulfonate (EMS), a process-related impurity which is a potential human carcinogen. Available at http://www.fda.gov/medwatch/safety/2007/safety07.htm#Viracept. September 10, 2007.

2. Dear Health Care Professional Letter. VIRACEPT® (nelfinavir mesylate) 250 mg, 625 mg tablets, and Powder for Oral Suspension – Important information for prescribers. Pfizer Inc., September 10, 2007.

3. Panel on Antiretroviral Guidelines for Adult and Adolescents. Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents. Department of Health and Human Services. October 10, 2006; 1-113. Available at http://aidsinfo.nih.gov/contentfiles/AdultandAdolescentGL.pdf. Accessed September 13, 2007.

4. DHHS Perinatal Panel Notice on Nelfinavir FDA-Pfizer Letter. Available at http://aidsinfo.nih.gov/contentfiles/PeriNFVNotice.pdf. September 11, 2007.

5. DHHS Pediatric Panel Notice on Nelfinavir FDA-Pfizer Letter. Available at http://aidsinfo.nih.gov/contentfiles/PedNFVNotice.pdf. September 11, 2007.