Interim Statement Regarding Potential Fetal Harm from Exposure to Dolutegravir – Implications for HIV Post-exposure Prophylaxis (PEP)

A preliminary unscheduled analysis of data from an ongoing NIH-funded observational study in Botswana suggests that an increased risk of neural tube defects was associated with exposure to antiretroviral (ARV) regimens that include dolutegravir (DTG) at conception.[i,ii,iii]

CDC makes the following interim recommendations for the use of HIV PEP (occupational or nonoccupational) while the agency prepares a more detailed review of the evidence and recommendations.

Health care providers prescribing PEP should **avoid use of DTG for:**

- **Non-pregnant women of childbearing potential who are sexually active or have been sexually assaulted and who are not using an effective birth control method; and,**
- **Pregnant women early in pregnancy** since the risk of an unborn infant developing a neural tube defect is during the first 28 days.

The preferred PEP regimen for these women is raltegravir, tenofovir, and emtricitabine.[iv,v] However, individual circumstances may dictate consideration of alternatives (e.g., raltegravir is not available). Health care providers seeking advice can call the National Clinical Consultations Center's PEPline at (888) 448-4911.

CDC currently recommends that prior to starting PEP all women of childbearing potential should have a pregnancy test performed.[iv,v] If the PEP regimen for a non-pregnant woman of childbearing potential must include DTG , she should use an effective birth control method until the PEP regimen is completed. Guidance for health care providers regarding contraceptive options for women can be found here: https://www.cdc.gov/reproductivehealth/contraception/contraception_guidance.htm.

Insufficient dietary folate can increase risk for neural tube defects. All women who are of childbearing potential, regardless of pregnancy status, should be provided at least 400 mcg of folic acid daily. Further information regarding folate for women who may become pregnant or are pregnant can be found here: https://www.cdc.gov/ncbddd/folicacid/recommendations.html. If DTG exposure occurs during pregnancy, especially in the first trimester, the pregnancy should be monitored for neural tube defects.

Health care providers should report all exposures to ARV medications, including exposures for all women who were pregnant or conceived and used PEP, to the Antiretroviral Pregnancy Registry (http://www.apregistry.com; 1-800-258-4263).

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[i] World Health Organization. Statement on DTG – Geneva 18 May 2018. http://www.who.int/medicines/publications/dugalets/Statement_on_DTG_18May_2018finaua=1

[ii] Food and Drug Safety Administration. FDA Drug Safety Communication: FDA to evaluate potential risk of neural tube birth defects with HIV medicine dolutegravir (Juluca, Tivicay, Triumeq) [Safety Announcement]. https://www.fda.gov/Drugs/DrugSafety/ucm608112.htm

[iii] The Panel on Antiretroviral Guidelines for Adults and Adolescents, the Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV, and the Panel on Treatment of Pregnant Women Living with HIV and Prevention of Perinatal Transmission. https://aidsinfo.nih.gov

[iv] Dominguez, KL, Smith DK, Thomas V, Crepaz N, Lang KS, et al. Updated Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Nonoccupational Exposures to HIV—United States, 2016. 1-91. https://stacks.cdc.gov/view/cdc/38856

[v] Kuhar DT, Henderson DK, Struble KA, Heneine W, Thomas V, Cheever LW, et al. Updated US Public Health Service guidelines for the management of occupational exposures to human immunodeficiency virus and recommendations for postexposure prophylaxis. *Infect Control Hosp Epidemiol* 2013;34:875–892. https://www.ncbi.nlm.nih.gov/pubmed/23917901