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July 17, 2018

Advisory: Use of Dolutegravir in Adults and Adolescents with HIV Who Are Pregnant or of Child-Bearing Potential and for Women Following Exposure to HIV-1 in the Occupational and Non-Occupational Setting and After Sexual Assault

Dear Colleague:

On May 18, 2018 the U.S. Food and Drug Administration (FDA) issued a Drug Safety Communication on the potential risk associated with the antiretroviral medication dolutegravir (DTG) and neural tube birth defects.¹ Dolutegravir is an HIV-1 integrase inhibitor. Dolutegravir, used in combination with other antiretroviral drugs, is a mainstay of both HIV-1 treatment and HIV-1 post-exposure prophylaxis (PEP). Dolutegravir is available as a single agent under the brand name Tivicay or as part of multidrug antiretroviral formulations under the brand names Juluca and Triumeq.

The FDA safety issuance, along with others issued by the World Health Organization (WHO)², United States President's Emergency Plan for AIDS Relief (PEPFAR)³, and European Medicines Agency (EMA)⁴, followed an unscheduled preliminary analysis of an ongoing U.S. National Institutes of Health (NIH) funded birth surveillance study in Botswana.

The analysis from the Botswana study indicated an increased risk of neural tube defects among infants of women who became pregnant while taking DTG-based regimens. The study reported 4 cases of neural tube defects out of 426 infants born to women who became pregnant while taking DTG-based regimens. This approximate 0.9% rate compares to a 0.1% risk of neural tube defects among infants born to women taking non-DTG-based regimens at the time of conception.¹ The same study has yet to find evidence of neural tube defects among infants born to women who initiated DTG-based regimens during pregnancy. Surveillance is ongoing for the additional pregnant women in Botswana who were exposed to DTG at time of conception; their deliveries will be monitored closely over the next 9 months (May 2018 – February 2019), and results are expected to be known soon thereafter.²

In response to these preliminary findings and alerts, the Medical Care Criteria Committee of the New York State Department of Health AIDS Institute's Clinical Guidelines Program⁵ is making the following recommendations for treatment of adults and adolescents with HIV who are pregnant or of child-bearing potential:

- When a woman presents for care within the first 8 weeks of pregnancy (dated by last menstrual period) and is taking dolutegravir (DTG), clinicians should:
 - Inform the woman about the potential risk of neural tube defects.
 - Offer the opportunity to change her antiretroviral therapy (ART) regimen.

- Offer her the option of ultrasound scans to assess neural tube closure, as follows:
 - Between 8 and 14 weeks (dating ultrasound)
 - And again, between 18 and 20 weeks (fetal anomaly scan)
- Clinicians should inform women taking DTG who present for care after 8 weeks gestation that the neural tube is closed by the end of the first trimester, and the risk to the fetus posed by a change in the maternal ART regimen is greater than the benefit.

The Department of Health and Human Services Antiretroviral Guidelines Panels on Antiretroviral Guidelines have also issued relevant recommendations.⁶

In addition, the Clinical Guidelines Program is making the following post-exposure prophylaxis (PEP) recommendations for woman after exposure to HIV-1 in the occupational and non-occupational settings and after sexual assault:

- The preferred PEP regimen for pregnant women is tenofovir disoproxil fumarate + emtricitabine (lamivudine may be substituted for emtricitabine) plus raltegravir.⁷

Sincerely yours,



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1. <https://www.fda.gov/Drugs/DrugSafety/ucm608112.htm>
2. http://www.who.int/medicines/publications/drugalerts/Statement_on_DTG_18May_2018_final.pdf?ua=1
3. <https://www.pepfar.gov/press/releases/282221.htm>
4. http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2018/05/news_detail_002956.jsp&mid=WC0b01ac058004d5c1
5. Selecting an Initial ART Regimen <https://www.hivguidelines.org/antiretroviral-therapy/what-to-start>
6. Recommendations Regarding Use of Dolutegravir in Adults and Adolescents with HIV who are Pregnant or Of Child Bearing Potential <https://aidsinfo.nih.gov/guidelines/html/3/perinatal-guidelines/0>
7. PEP for HIV Prevention <https://www.hivguidelines.org/pep-for-hiv-prevention/>