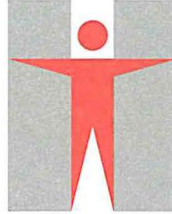


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Dear Healthcare Professionals,

Safety alerts on the risk of birth defects with the HIV medicine Dolutegravir
by EMA & U.S. FDA

Your attention is drawn to the following drug safety alerts announced by the European Medicines Agency (EMA) and U.S. Food and Drug Administration (FDA):

1. European Union: New study suggests risk of birth defects in babies born to women on HIV medicine dolutegravir – While EMA review is ongoing, dolutegravir should not be used in women seeking to become pregnant

The EMA's Pharmacovigilance Risk Assessment Committee (PRAC) is evaluating preliminary results from a study which found 4 cases of birth defects such as spina bifida (malformed spinal cord) in babies born to mothers who became pregnant while taking dolutegravir.

The study, which looked at babies born to 11,558 HIV-infected women in Botswana, showed that 0.9% of babies (4 of 426) whose mothers became pregnant while taking dolutegravir had a neural tube defect, compared with 0.1% of babies (14 of 11,173) whose mothers took other HIV medicines. Final results are expected in about a year. Women who have been prescribed dolutegravir should not stop taking their medicine without first consulting their doctor.

While EMA is assessing the new evidence it has issued the following precautionary advice:

- Dolutegravir HIV medicines should not be prescribed to women seeking to become pregnant.
- Women who can become pregnant should use effective contraception while taking dolutegravir medicines.

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aspire to be an internationally renowned public health authority*

EMA will update the recommendations as necessary when it concludes its assessment.

Please refer to the following website in EMA for details:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2018/05/news_detail_002956.jsp&mid=WC0b01ac058004d5c1

2. The United States: FDA Drug Safety Communication: FDA to evaluate potential risk of neural tube birth defects with HIV medicine dolutegravir (Juluca, Tivicay, Triumeq)

The U.S. FDA is alerting the public that serious cases of neural tube birth defects involving the brain, spine, and spinal cord have been reported in babies born to women treated with dolutegravir used to treat human immunodeficiency virus (HIV). Preliminary results from an ongoing observational study in Botswana found that women who received dolutegravir at the time of becoming pregnant or early in the first trimester appear to be at higher risk for these defects.

Neural tube defects are birth defects that can occur early in pregnancy when the spinal cord, brain, and related structures do not form properly. To date, in this observational study there are no reported cases of babies born with neural tube defects to women starting dolutegravir later in pregnancy. They are investigating this new safety issue and will update the public when they have more information.

Dolutegravir is an FDA-approved antiretroviral medicine used in combination with other antiretroviral medicines to treat HIV, the virus that can cause acquired immunodeficiency syndrome (AIDS). Dolutegravir works by blocking integrase, an HIV enzyme, to prevent the virus from multiplying and can reduce the amount of HIV in the body. Stopping dolutegravir without first talking to a prescriber can cause the HIV infection to become worse. Approved in 2013, dolutegravir has been on the market for 5 years, and is available as a single ingredient product under the brand name Tivicay and as a fixed dose combination tablet with other HIV medicines under the brand names Juluca and Triumeq.

Ongoing monitoring will continue as part of the observational study in Botswana. Additional birth outcomes are projected from pregnant women who were exposed to dolutegravir at the time of becoming pregnant. They will conduct a comprehensive review of the results and any other data that becomes available. They will update the public with any new information.

Please refer to the following website in US FDA for details:

<https://www.fda.gov/Drugs/DrugSafety/ucm608112.htm>

In Hong Kong, there are 2 registered pharmaceutical products containing dolutegravir, namely Tivicay Tablets 50mg (HK-63516) and Triumeq Tablets (HK-64012). Both products are registered by Glaxosmithkline Limited, and are prescription-only medicines. So far, the Department of Health (DH) has received 3 cases of adverse drug reaction related to dolutegravir, but these cases were not related to birth defects. In the light of above EMA and FDA's announcements, the DH will keep vigilant on any further updates on the products issued by other health authorities. Healthcare professionals are advised to balance the risk of possible adverse effects against the benefit of treatment.

Please report any adverse events caused by drugs to the Pharmacovigilance Unit of Department of Health (tel. no: 2319 2920, fax: 2319 6319 or email: adr@dh.gov.hk). For details, please refer to the website at Drug Office under "ADR Reporting": <http://www.drugoffice.gov.hk/adr/html>. You may wish to visit the Drug Office's website for subscription and browsing of "Drug News" which is a monthly digest of drug safety news and information issued by Drug Office.

Yours faithfully,



(Joseph LEE)

for Assistant Director (Drug)